RISK FACTORS OF AVASCULAR NECROSIS OF FEMORAL HEAD IN A TERTIARY HEALTH CARE

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Dedicated

To

My Family

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ABBREVIATIONS

AVN	Avascular necrosis
HDL-C	High-density lipoprotein cholesterol
HIV	Human Immunodeficiency Virus
IDF	International Diabetes Federation
MS	Metabolic syndrome
MRI	Magnetic resonance imaging
NMS	Non metabolic syndrome
SLE	Systemic lupus erythematosus
SCD	Sickle cell disease
TG	Triglycerides

ABSTRACT

Introduction: Avascular necrosis is defined as a group of symptoms, dominated by pain, loss of function and bony collapse caused by anoxemia and other deficiency in arterial nutrition of the head of the femur, prolonged enough to result in the marked degeneration, even necrosis of bone. There are limited studies on the epidemiology of AVN of femoral head in Indian population. This study was designed to investigate for the risk factors of AVN hip and to assess the severity as per radiological staging.

Materials and Methods: 60 patients (95 hips) of AVN who were evaluated at our center between September 2018 to June 2020 were included in this prospective study. The details of history, clinical examination and radiological grading were entered into a proforma.

Results: The mean age was 46.7 years (range 21-72 years) and 46.6% (*n*=27) patients were between 21 and 40 years. Male to female ratio was 4:1. Bilateral AVN was observed in 58.3% (*n*=35) patients. Alcohol consumption (42.3%) was most commonly observed followed by Steroid administration (35%) and idiopathic in (18.3%) patients. Among patients with a history of steroid intake, Brochial asthma was reported most frequently (33.3%) as the underlying disease. According to Ficat and Arlet classification, it was observed that patient presented with advanced disease. There were 69 hips (71.5%) with grade III and grade IV. None of our patient was presented with grade I. The prevalence of metabolic syndrome was 53.3% in this study.

Conclusion: AVN in the Indian patients is a disease of young individuals with male predominance. Alcohol consumption (42.3%) is most commonly observed cause among the patients suffering from AVN of femoral head followed by Steroid administration (35.0%). No identifiable risk was observed in 18.3% of patients. The steroid induced AVN are usually bilateral, whereas Alcohol induced AVN has equal incidence of unilateral and bilateral involvement. In Idiopathic AVN, incidence of unilateral disease was observed.

Keywords: Avascular necrosis, Femoral head, Hip joint, Risk factor, Metabolic syndrome.

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INTRODUCTION

Avascular necrosis is defined as a group of symptoms, dominated by pain, loss of function and bony collapse caused by anoxemia and other deficiency in arterial nutrition of the head of the femur, prolonged enough to result in the marked degeneration, even necrosis of bone. Its most frequent cause is abrupt disruption, thrombosis or embolism of a large amount of coronary artery[1]. Koenig was the first to describe this condition, which he termed osteochondritis dissecans, in 1888. In 1925, Haenish described the first case that involved the femoral head. In 1940, the cause of the necrosis was deemed to be arterial occlusion. Pietrograndi described the first case of femoral head AVN after steroid use in 1957. Avascular necrosis is also referred to as "AVN", "aseptic necrosis" and "ischemic bone necrosis"[1].

It is a progressive devastating disease with wide ranging etiology and poorly understood pathogenesis commonly affecting patients in the third, fourth, or fifth decade of life. The development of AVN can have a major impact on an individual's lifestyle. The bones commonly affected are, the femoral head, humeral head, scaphoid, lunate, talus, medial condyle of tibia and capitellum, of which the femoral head is the commonest site. AVN can occur in a single bone, but more commonly occurs in several bones at one time (multifocal AVN)[2].

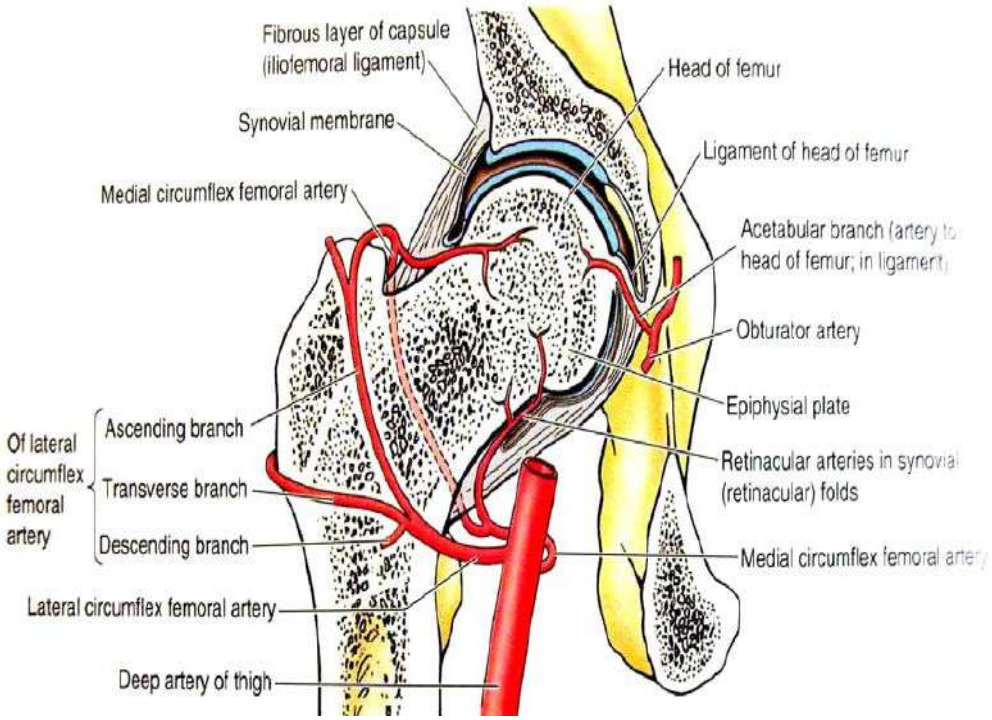
AVN can sometimes be disabling, depending on what part of the bone is affected, how large an area is involved, and how well the bone rebuilds itself. Normal bone continuously breaks down and rebuilds itself. This process keeps the bones strong. AVN is the result of bone tissues breaking down faster than the body can repair them. If the disorder progresses, it can lead to pain and arthritis[2].

Vascular Anatomy Of Femoral Head

Crock divided the arterial supply of femur head into three major groups.

1. An extracapsular arterial ring located at the base of the femoral neck.
2. Ascending cervical branches of the extracapsular arterial ring on the surface of the femoral neck.
3. The artery of the ligamentum of teres.

Picture 1- Anterior view of coronally sectioned hip joint



The extracapsular arterial ring and the ascending retinacular vessels are derived from the medial and lateral circumflex femoral arteries. The medial circumflex artery gives of small inferior retinacular (medial ascending) artery. It gives branches to the femoral neck and then passes over the epiphyseal growth plate to enter the capital femoral epiphysis in children.

Posteriorly, the medial circumflex femoral artery communicates with branches of superior gluteal artery and gives off small Posterior retinacular arteries. The termination of medial circumflex femoral artery becomes the superior retinacular (lateral ascending) artery, which supplies the greatest portion of blood to the head of femur in adults and the capital femoral epiphysis in children. This artery penetrates the capsule in the trochanteric notch (an extremely narrow space between the greater trochanter and femoral neck) and is therefore vulnerable to injury in fractures of neck of femur.

The lateral circumflex femoral artery usually arises from the Profunda

femoris artery. It give the anterior retinacular (anterior ascending) branch to the proximal femur. The lateral circumflex femoral artery communicates with the medial circumflex femoral artery in the trochanteric fossa, completing the extracapsular arterial ring. The anterior portion of this ring is thus derived primarily from the lateral circumflex femoral artery, whereas the medial, posterior and lateral portions branch from the medial circumflex femoral artery.

The branches of the ascending retinacular arteries form a subsynovial anastamotic intraarticular arterial ring at the margin of the articualar cartilage of femoral head. The artery of the ligamentum teres contributes only a small portion of the arterial blood supply to the center of the femoral head.

Prevalence

AVN of femoral head is a relatively common ailment, accounting for 10% or more of around half a million joint surgeries practiced in the United States per year[2]. The age of 75% of the patients with AVN ranges between 30 and 50 years. Its prevalence is twice in men than in women with a male to female ratio of about 7:3[3]. Patients with systemic lupus erythematosus (SLE) are an exception to this gender ratio[4].

Etiology

Wide arrays of risk factors for the development of AVN of the femoral head have been recognized. Such risk factors include corticosteroid use, alcohol, trauma, hypercoagulable states. However, much of the etiology of the disease is somewhat unclear. In general terms, the causes of AVN encompass the interruption of blood supply to the bone and consequent ischemia, due to local trauma or non- traumatic systemic conditions. Among the traumatic causes of AVN are: burns, fractures, dislocations, and vascular trauma.

Table 1- Common causes of AVN[3].

Direct causes	Indirect causes	Rare causes
Trauma	Corticosteroids	Polyarteritis
Irradiation	Alcohol abuse	Thalassemia
Hematologic Disorders	Idiopathic	Carbon poisoning tetrachloride
Cytotoxins	Thrombophilia	Hyperlipidemia
Gaucher disease	Hypofibrinolysis	Cushing's disease
Sickle cell disease	SLE, other autoimmune disorders	Pregnancy
	Renal insufficiency	
	Organ Transplantation	
	Hemophilia	

It is widely recognized that the lack of blood flow to the bone is the common denominator for the development of AVN. If the cause is traumatic in nature, then the physical interruption of regular blood supply is the event leading to necrosis. Whereas if the etiology is non-traumatic, the pathogenesis is not always as straight forward. The process will depend on the underlying condition and may or may not comprise coexisting morbidities. While many risk factors for developing AVN have now been acknowledged, they do not necessarily predict the disease or its outcome. AVN is rather, a multifactorial on-going condition as we will further discuss in the pathogenesis-related section.

Pathophysiology

Extraosseous arterial factors are the most important. The femoral head is at increased risk because the blood supply is through end arteries with poor collateral development. Blood supply can be interrupted by trauma, vasculitis (Raynaud disease) and vasospasm (decompression sickness)[5]**.**

Intraosseous arterial factors may block the microcirculation of the femoral head through circulating microemboli. These can occur in sickle

cell disease, fat embolization or air embolization from dysbaric phenomena[5].

Intraosseous venous factors affect the femoral head by reducing venous blood flow and causing stasis. These factors may accompany conditions such as Caisson disease, SCD or enlargement of intramedullary fat cells[5].

Intraosseous extravascular factors affect the hip by the increasing the pressure, resulting in a femoral head compartment syndrome. Fat cells hypertrophy after steroid administration or abnormal cells, such as Gaucher and inflammatory cells, can encroach on intraosseous capillaries, reducing intramedullary circulation and contributing to compartment syndrome. Repeated microfractures in the weight bearing segment of the femur may cause multiple vascular lesions resulting in ischemia within fragile and poorly repaired bone[5].

Extraosseus extravascular (capsular) factors involve the tamponade of the lateral epiphyseal vessels located within the synovial membrane, through increased intracapsular pressure. This occurs after as trauma, infection, and arthritis, causing effusion that may affect the blood supply to the epiphysis[5].

According to Kenzora the term avascular necrosis should be reserved exclusively for the post-traumatic group, because they originate in ischemia as a result of interruption of blood flow. When the etiology of the necrosis has not been established clearly, or it is obscure it is best to call in idiopathic AVN[6].

Metabolic syndrome is known to be a cluster of interrelated risk factors of metabolic origin such as elevated blood pressures, glucose metabolism disturbances, dyslipidemia, and obesity[7]. The exact mechanisms of the complex pathways of metabolic syndrome are under investigation. The pathophysiology is very complex and has been only partially elucidated. Most patients are older, obese, sedentary, and have a degree of insulin resistance. Stress can also be a contributing factor. The most important risk factors are diet (particularly sugar-sweetened beverage consumption), genetics, aging, sedentary behavior or low physical activity, disrupted chronobiology/sleep, mood

disorders/psychotropic medication use, and excessive alcohol use.

Prevalence of the metabolic syndrome varies across the world, in part reflecting the age and ethnicity of the populations in the globe studied and the diagnostic criteria applied. The global burden of Metabolic Syndrome is 20-25% and in India the prevalence is 19%. The metabolic syndrome is associated with a 2-fold increase in cardiovascular outcomes and a 1.5-fold increase in all-cause mortality[8].

Definitions of metabolic syndrome:-

IDF (International Diabetes Federation)[9]

According to the new definition, for a person to be defined as having the Metabolic syndrome, they must have central obesity (defined as waist circumference:- Male ≥ 90 cm & Female ≥ 80 cm) plus any two of four additional factors. These four factors are:

- Raised triglycerides: > 150 mg/dL (1.7 mmol/L), or specific treatment for this lipid abnormality
- Reduced HDL cholesterol: < 40 mg/dL(1.03 mmol/L) in males, < 50 mg/dL (1.29 mmol/L) in females, or specific treatment for this lipid abnormality
- Raised blood pressure (BP): systolic BP > 130 or diastolic BP >85 mm Hg, or treatment of previously diagnosed hypertension
- Raised fasting plasma glucose (FPG): >100 mg/dL (5.6 mmol/L), or previously diagnosed type 2 diabetes

WHO

The World Health Organization 1999 criteria[9] require the presence of any one of diabetes mellitus, impaired glucose tolerance, impaired fasting glucose or insulin resistance, AND two of the following:

Blood pressure: ≥ 140/90 mmHg

- Dyslipidemia: triglycerides (TG): ≥ 1.695 mmol/L and high-density lipoprotein cholesterol (HDL-C) ≤ 0.9 mmol/L (male), ≤ 1.0 mmol/L (female)
- Central obesity: waist:hip ratio > 0.90 (male); > 0.85 (female), or body mass index > 30 kg/m2
- Microalbuminuria: urinary albumin excretion ratio ≥ 20 µg/min or

albumin: creatinine ratio ≥ 30 mg/g

Diagnosis of AVN

Currently, there is a better understanding of the natural history of symptomatic AVN and how it progresses, than the myriad of the commonly associated factors responsible for its development. Surprisingly, many patients with AVN often develop the disease within few months of exposure to a particular risk factor, whereas other patients never develop AVN when exposed to that same risk factor. The more knowledge we are able to acquire regarding the natural history of AVN would allow us to better understand disease prognosis and outcomes so that management results in the best line of therapy for a given patient.

Symptoms associated with AVN

AVN of the femoral head may lead many different courses mainly depending on the site and size of the ischemic structure. The presenting symptom is usually pain, which may be initially mild or as happens with more insidious onsets, the pain may be vague, making the diagnosis less evident. On the other hand, when the cause is traumatic, the pain may be of rapid onset and severe[10]. In cases where ischemia is extensive, infarction of the bone causes very intense pain and is usually the result of predisposing conditions such as sickle cell hemoglobinopathies, lipid storage diseases, etc.[11].

Initially, non-traumatic AVN may be asymptomatic, and the duration of this stage may be variable[12]. It seems that in many cases the pathophysiology of pain is related to the increase in pressure inside of the bone structure. Although pain may also be the result of synovial effusions, degenerative arthritis, etc., it is crucial to determine the etiology of the pain in order to successfully resolve the cause with precise treatment.

In AVN of the femoral head, pain usually involves the groin or anterior thigh area. Frequently, the disease is unilateral but may become bilateral in 55% of the patients over the course of 2 year. Pain may further be induced by joint mobilization, until it becomes present even at rest for which analgesics are commonly prescribed. Mechanical

function of the joint may be initially preserved but as the disease progresses, motion may become limited and painful. Many times, limping may be present in otherwise radiographically normal subjects. Some studies have reported that symptomatic AVN lesions appearing at the weight-bearing regions of the femoral head show high rates of collapse[13,14]. Additionally, development of subchondral fractures usually predicts posterior collapse. Collapse of the articular surface is an irreversible event occurring in the natural history of AVN. This collapse commonly presents with concomitant pain, installment of osteoarthritis, and a poor prognosis.

Imaging diagnosis of AVN

Plain film radiography:

Using plain film, the sensitivity for detecting early stages of the disease is as low as 41%[15]. Plain film does not detect stage 0 and I AVN. A delay of 1-5 years may occur between the onset of symptoms and the appearance of radiographic abnormalities. Normal radiographic findings do not necessarily mean that disease is not present.

Although still considered the basic initial imaging for suspected AVN, radiographs exhibit high specificity for advanced disease but low sensitivity for early disease. Portrayal of early disease is crucial given that early diagnosis is directly related with better prognoses as it has been found in various studies that once radiographic diagnosis of AVN is made, collapse usually occurs within 2 years in 32–79 % of patients[16,17].

Magnetic resonance imaging (MRI)

Imaging by magnetic resonance is considered the method of choice for detecting and staging AVN due to its multiplanar imaging, outstanding soft tissue contrast, and the ability to discriminate fat from other bone marrow tissues[18]. Compared to other imaging methods such as plain radiography or computed tomography, magnetic resonance imaging (MRI) has been found to have the highest sensitivity and specificity[19]. It is a practical tool for early diagnosing, quantification of the extent of the lesion within the femoral head and for its further stratification [20].

Magnetic resonance imaging has recently emerged as the most

sensitive, specific, and widely used diagnostic tool for avascular necrosis of femoral head. In most reports, MRI can diagnose very early lesions with a greater than 90 percent specificity and sensitivity based on histology or eventual progression[21]. Screening of asymptomatic, high-risk patients may enable early intervention.

Classification systems of AVN

Based on clinical and radiological features of AVN different staging systems have been developed. In 2006, Mont et al. published a systematic review of the literature where they reported the 16 major systems used to classify AVN[22]. Out of all them, the most widely used appears to be the Ficat classification which accounted for more than 63% of the reported studies. Other three widely spread classification systems were the University of Pennsylvania System (20%), the Association Research Circulation Osseous (ARCO) system (12%) and the Japanese Orthopaedic Association System (5%).

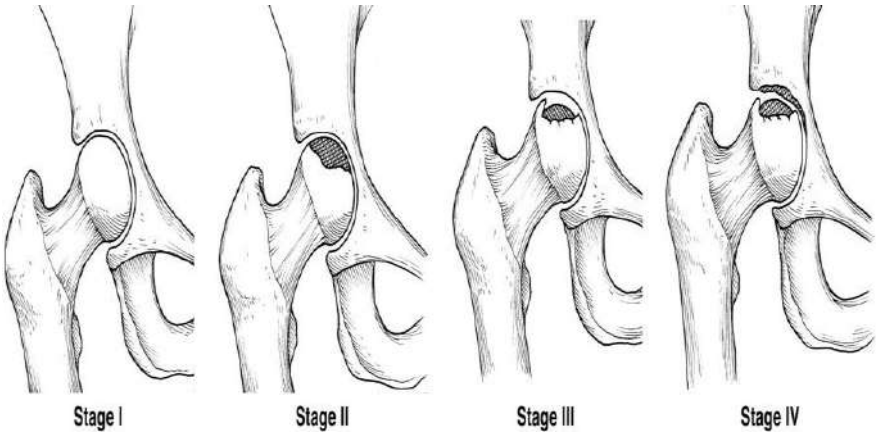
FICAT and ARLET Classification

Ficat and Arlet developed this classification system in the 1960s[22]. It originally had three stages and it has been modified at least four times. In the present day, most physicians will refer to the four-stage system that is rather simple.

Table 2- Ficat and Arlet Classification[22]

STAGE	PAIN	X RAY	MRI
I	✚	Normal	✚
II	✚	Diffuse sclerosis, cysts	✚
III	✚	Subchondral fracture (crescent sign; with or without head collapse)	✚
IV	✚	Femoral head collapse, acetabular involvement and joint destruction (osteoarthritis)	✚

Picture 2- Ficat and Arlet Classification



ARCO Classification

The Association Research Circulation Osseous (ARCO) classification[22] system is more practical from a clinical point of view as it allows, not only to establish the prognosis and follow-up of disease progression but also to establish the best line of therapy.

Table 3- ARCO Classification[22].

STAGE	X RAY	MRI	LOCATION	EXTENSION
0	Normal	−	No	No
I	Normal	+	Medial Central Lateral	Mild (<15% femoral head) Moderate (15-30%femoral head) Severe (> 30% femoral head)
II	Sclerosis osteolysis, focal porosis	+		
III	Crescent sign and/or flattening of the articular surface	+		
IV	Osteoarthritis	+	No	No

Picture 3- Crescent sign

Picture 6- Ficat & Arlet stage IV of femoral head avascular necrosis

Literature from the western world and Asian countries report chronic alcohol consumption and steroid administration as the most common etiologies.[22-31]. Intriguingly enough, in the context of AVN, studies investigating at risk factor associated with AVN of femoral head in these patients as well as delineating correlation were limited. To fill in this knowledge gap, a study of this order was necessary. Thus a study designed to study the possible risk factor of avascular necrosis of the femoral head was necessary because very few such studies has been done in India especially. Being the tertiary care hospital and as a referral hospital for several district hospital, it represents the pattern of AVN of femoral head in India.

AIMS AND OBJECTIVES

Finding the risk factors associated with the development of avascular necrosis of the femoral head.

REVIEW OF LITERATURE

Kang et al conducted a study to estimate the prevalence of AVN of the femoral head in Korea. Using medical claims data from the Korean National Health Insurance Corporation, all individuals treated under a diagnosis of AVN of the femoral head were identified for each year from 2002 to 2006. Among them, the number of true cases was estimated using a randomly collected validation sample of 382 patients for which the actual diagnosis was investigated by authors. Males predominated in this study. They found that 32.4% had history of alcohol abuse, and 14.6% was related to steroid. Bilateral involvement was noticed in 37%. Besides arthroplasty, decompression was the most frequently performed joint-preserving procedure. They believe that the results serve as important baseline for understanding the disease[23].

Wang et at conducted a retrospective study of 643 AVN of the femoral head cases to analyze the potential causative factors, age, gender, latency period, time from the onset of pain to diagnosis, and Association Research Circulation Osseous stage. Of 643 cases, 315 cases were bilateral and 328 cases were unilateral, with an average age of (47.55 ± 15.27) years. In the steroid-induced group, the average age at symptom onset was (41.80 ± 15.47) years, and the median duration from taking steroid to the onset of pain was 36 months. In the alcohol-induced group, the average age at onset of symptoms was (48.06 ± 11.90) years and the median time of habitual alcohol use was 240 months. In the idiopathic group, the average age was (50.33 ± 15.88) years. Of the total of 958 hips, 647 were at stage III or IV. The stage at diagnosis was earlier in the steroid-induced group than in the alcohol-induced, traumatic, or idiopathic groups[24].

Fukushima et al conducted a nationwide epidemiologic survey in 2005. The survey included all orthopedic departments in Japan by stratified random sampling according to the number of beds. The number of patients who sought medical care for idiopathic AVN during 2004 was estimated to be 11,400 (95% confidence interval, 10,100-12,800). The peak in age distribution occurred in the 40s. Potential causative factors

were systemic steroid administration (51%) and habitual alcohol use (31%). Among patients younger than 40 years, steroid use was the most prominent potential causative factor (60%) and hip replacement frequently was performed (45%). A greater proportion of patients with no history of steroid or alcohol use was observed among patients 65 years or older (41%). This study concluded that the importance of developing preventive and treatment strategies, especially among the younger population[25].

Cooper et al conducted a case-control study to examine the incidence of AVN of femoral head, patient characteristics and selected potential risk factors for AVN using health record databases in the UK. AVN cases (n = 792) were identified from 1989 to 2003 and individually matched (age, sex, and medical practice) up to six controls (n = 4,660) with no record of AVN. Annual incidence rates were computed, and a multivariable logistic regression model was derived to evaluate selected risk factors. AVN of the hip represented the majority of cases (75.9%). Statistically significant risk factors for AVN were systemic corticosteroid use in the previous 2 years, hospitalization, referral or specialist visit, bone fracture, any cancer, osteoporosis, connective tissue disease, and osteoarthritis within the past 5 years. This study provides further perspective on the descriptive epidemiology of AVN[26].

Hirota et al conducted a nationwide multicenter case-control study in Japan to investigate the association of alcohol intake, cigarette smoking, occupation and other factors with the development of idiopathic AVN of the femoral head. 118 cases with no history of systemic corticosteroid use were compared with 236 controls matched for sex, age, ethnicity, clinic, and date of initial examination. The risks of developing AVN associated with potential risk factors were estimated by adjusted relative odds obtained by a conditional logistic regression model. The elevated relative odds were observed for occasional drinkers and regular drinkers with a significant dose-response relation. An increased risk was found for current smokers but a linear increasing trend in the cumulative effect of smoking was not evident at 20 pack-years or over. A weak but significant dose-response relation was

observed for daily occupational energy consumption ($p < 0.05$). This study confirmed the strong association of alcohol intake and positive association of cigarette smoking and suggested the role of heavy physical work[27].

Matsuo et al conducted a study 112 patients with idiopathic AVN of the femoral head having no history of systemic corticosteroid use and compared them with 168 hospital controls. Patients and controls were matched for gender, age, ethnicity, hospital, and time of initial diagnosis. The role of alcohol intake, cigarette smoking, and occupational status was assessed in relation to the development of AVN. An elevated risk for regular drinkers and a clear dose-response relationship was noted. A significantly increased risk was found for current smokers. However, the cumulative effect of smoking was not evident. No increased risk was found for obesity or for heavy physical work. This study confirmed the consistent association with excessive alcohol intake and suggested the immediate untoward effects of smoking[28].

Hanumantharaya et al studied the etiological factors and treatment protocol of AVN of femoral head in 20 patients. Pre-clinical studies includes model of AVN, variety and dosage of steroid consumption, histologic and imaging analyses. Clinical studies includes study design, classification and etiology of AVN, and treatment protocol. It was noticed that according to classification by Steinberg et al 9 hips (28.13) with stage III, 8 hips (25%) with stage II and 2 hips (6.25%) associated with stage I disease. There was one hip (3.13) of Stage V and VI each. This study concluded that a focus on early disease management aimed at joint preservation by preventing or delaying progression is key[29] .

Jacobs took 164 patients with alcoholism-induced AVN in his study over a 22-year period, from 1962 to 1984. In this study, the presence of AVN was diagnosed in patients aged 21-67 years. 28% of patients were found under 40 years of age and 76% were found under 50 years. Bilateral hip necrosis was present in 44.5% of patients and within three years of the diagnosis with AVN of femoral head, the presence of multifocal necrosis became evident in 23 cases at sites away from the hip (shoulders and knees). Hyperlipidemia was found in 38.4% of cases

involving both cholesterol and triglycerides. This paper supports the hypothesis that co-existent hyperlipidemia is linked to alcoholism induced bone necrosis[30] .

Vardhan et at studied the risk factors of AVN of femoral head and assess the severity of disease as per radiological staging (Association Research Circulation Osseous) and clinical score (Harris hip score). 249 patients (382 hips) of AVN were evaluated in this retrospective study. The mean age was 34.71 years and 70.28% patients were between 20 and 40 years. Male to female ratio was 5:1. Bilateral involvement was seen in 61.61%patients. Steroid administration 37.3% was most commonly observed in the patients followed by idiopathic in 21.3% patients, chronic alcohol consumption in 20.1% patients and trauma in 15.3% patients. There were 48% hips in ARCO Stage 2 followed by 33% in Stage 3 and 16% in Stage 4. This study concluded that steroid intake is most commonly observed in these patients followed by idiopathic, chronic alcohol consumption and trauma[31].

Koch et al studied the prevalence of metabolic disorders in 70 patients with AVN of femur head. 28 patients were found with history of large-dose steroid therapy, chronic alcoholism and radiation. As a result of the biochemical blood examination in 29 patients with hyperlipoproteinemia and 25 patients with dyslipidemia were determined, accompanied by a carbohydrate metabolic disturbance (15 cases) and a purine metabolic disturbance (13 cases)[32].

Zhao et al conducted a study to investigate the prevalence of AVN of femoral head and its associated risk factors in the Chinese population. 30,030 participants underwent a questionnaire investigation, physical examination, lipid profile investigation and X-ray or MRI of hip joint. AVN was diagnosed in 218 subjects (0.725%) and the estimated AVN cases were 8.12 million among Chinese people aged 15 years and over. The prevalence was significantly higher in males than in females. This study showed that high blood levels of triglycerides, total cholesterol, LDL cholesterol, and non HDL cholesterol, male, urban residence, family history of AVN, heavy smoking, alcohol abuse and glucocorticoid intake, overweight and obesity were all significantly associated with an

increased risk of AVN of femoral head[33] .

Puhl et al studied 100 patients suffering from AVN were subjected to comprehensive clinical, roentgenologic and chemical laboratory examination. Disturbance of lipid metabolism was found in 41% of the patients related to abnormal liver function blood report and history of alcohol abuse. The statistically significant correlation of these factors makes it probable that there is actually a pathogenetic chain abuse of alcohol-hyperlipoproteinemia-arteriosclerosis-AVN and metabolic disturbances are mostly linked with hyperlipoproteinemia[34].

Zsernaviczky et al studied the relation between AVN of the femoral head and the primary disturbance of fat metabolism type II hypercholesterolemia. Type II hypercholesterolemia is of particular importance since it produces early atherosclerosis which demands early diagnosis, since this condition can be treated by drugs and diet. This study concluded that differentiation of dyslipidemia and hyperlipidemia in AVN of the femoral head will enable us to define signs of disturbances of lipid metabolism and AVN is a late complication of a differentiated fat-metabolic disturbance**.**[35].

Kuga conducted a study of 336 patients with alcoholic liver dysfunction who had radiographic examination of the hip for alcohol abuse treatment in Japan, the records for 291 men and 1 woman (mean age, 47.8 years; range, 24 to 72 years) had adequate information available concerning daily and cumulative alcohol intake, duration of intake, serum concentrations of liver enzymes, and platelet count. These variables were investigated for any correlation between the 8 patients with radiographic evidence of AVN and the 284 without AVN. These results suggested that AVN occurred in the late stages of liver disease when serum enzyme concentrations had returned to normal or were only mildly elevated[36].

Chao et al in 2003 conducted a study of alcohol metabolizing enzyme genes present in chinese alcoholics with avascular necrosis of the hip joint, pancreatitis and cirrhosis of the liver. It was concluded that there are multiple theories about the pathogenesis. Two of them are commonly mentioned 1. Thromboemboli in the blood supply to bone

resulting from circulating fat and 2. vessel occluded by excessive packing of the adjacent marrow spaces with extravasated blood or fat. It was found that combination of AVN and cirrhosis to be more prevalent than AVN and acute pancreatitis. This paper supports the hypothesis that the presence of dysfunction of carbohydrate and lipid metabolism was more prevelant in patient with AVN of bone and alcohol induced liver disease[37] .

Hedri et al conducted a study of 326 kidney transplant recipients to determine the frequency of AVN among kidney transplant recipients and the risk factors by comparing them with a population without AVN. 15 patients developed AVN with mean age of 40.86 years including 11 men and 4 women. Fifteen kidney transplant recipients without AVN were selected to be matched for age, gender and date of transplantation (control group). AVN was diagnosed at a mean of 3.5 years after transplantation (range, 0.5-13 years). The main localization of AVN was the femoral head in 12 cases and the femoral condyle in 3 cases. Statistical analysis showed that the cumulative steroid dose and the acute rejection rate were higher among the AVN group than the control group (P=.04 and P=.058, respectively). The prevalence of AVN in our population is 4.6% which is probably an underestimate since these were symptomatic cases. This study showed that reduction or early withdrawal of steroids is the only efficient preventive treatment for AVN[38].

Koo et al conducted a study to determine the onset of AVN of the femoral head following steroid treatment. Medical record data of patients with steroid-related AVN of the femoral head were reviewed. 22 patients were diagnosed with AVN (8 male and 14 female patients ranging in age from 17 to 60 years). The total dose of steroid which was used until the time of detection of AVN by MRI ranged from 1800 to 15,505 mg prednisolone or its equivalent (mean 5928 mg). The period from the start of steroid treatment to the diagnosis by MRI ranged from 1 month to 16 months (mean 5.3 months). The duration of steroid treatment within this period ranged from 1 month to 12 months (mean 4.5 months). This study showed that close observation and more

aggressive screening are recommended within the first year of long-term steroid treatment to prevent advanced AVN of the femoral head[39] .

Griffith et al. found that twelve (5%) of 254 patients with SARS had evidence of AVN of the femoral head and that the cumulative prednisolone-equivalent dose was the most important risk factor with the risk being 0.6% for patients receiving a dose of <3 g and 13% for those receiving a dose of >3 g. The risk period for the development of AVN of the femoral head following corticosteroid therapy has been more exactly defined[40].

Sakamoto et al Using magnetic resonance imaging, prospectively evaluated the femoral heads in forty-eight patients (ninety-six hips) receiving high-dose corticosteroids for various autoimmune-related disorders. Abnormalities were found in thirty-one hips (32%). The initial necrotic changes were seen as well-demarcated, band-like zones at a mean of 3.6 months (maximum, twelve months) after initiation of the corticosteroid treatment[41].

Fink et al, in their prospective study of forty-three patients receiving corticosteroids while undergoing renal transplantation observed that AVN of the femoral head occurred in six hip joints of four patients (9%) within three months after the transplantation. Magnetic resonance imaging performed twelve months after transplantation revealed no additional lesions[42].

Matsuo et al in their study, compared 112 patients with AVN of the femoral head with 168 control patients and found an elevated risk for regular drinkers (>8 mL of alcohol every day) (relative risk = 7.8). They also reported a clear dose-response relationship with relative risks of 3.3, 9.8, and 17.9 for current drinkers consuming <400, 400 to 1000, and ≥1000 mL/wk of alcohol, respectively[43].

Wen et al found that compared to non-smokers, current smokers had a higher risk of developing AVN showing odds ratios of 2.5; as well as former smokers who displayed OR of 1.82. The current smokers were further classified as heavy (>20 cigarettes/day) and light smokers (<20 cigarettes/day). Both demonstrated higher risk of AVN than

non-smokers. When the patients were categorized by pack-years to evaluate the impact of time of exposure to tobacco smoke, the heavy smokers (>20 packs-years) showed higher risk than the non-smoker group but this was not the case for the light smokers (<20 packs-year) that displayed no significant greater risk than non-smokers. They concluded that these findings suggest that current smokers are at a higher risk of AVN, which persists even after having quit and that heavy cigarette smoking confers a higher risk of AVN than light smoking[44] .

Adesina et al conducted a study in which California's Office of Statewide Planning and Development discharge databases (1991-2013) was used to identify and estimate factors associated with AVN diagnosis. The cumulative incidence of AVN to age 30 years was higher among patients with more severe sickle cell disease (24%; vs 8% in less severe). From 2003 to 2013, patients with more severe cases of sickle cell disease were more likely to develop AVN. Twenty seven percent of post hip surgery patients was readmitted within 30 days, mostly due to painful vaso-occlusive crises. This study concluded that AVN is a common sickle cell disease complication that increases with age; ongoing studies into prevention and effective nonsurgical interventions for sickle cell disease induced AVN must remain a high research priority[45] .

Miller et al conducted a study where they found that 4.4% of HIV-infected adults suffered from AVN and no evident hip lesions; such was not the case for the age and gender-matched control group. Hip lesions were more likely to occur in patients who received corticosteroids, lipid-lowering drugs, or testosterone. Although many studies have attributed the pathogenesis retroviral therapy itself[46]. A study by **Ries et al** have identified patients with AVN and no other associated risk factors, which would suggest that the HIV infection is in itself a risk factor for developing the condition[47].

MATERIAL AND METHODS

Source of date

This was prospective analysis of risk factor in patients with avascular necrosis of femoral head, conducted in patients who underwent treatment at Dayanand Medical College, Hospital.

Patients presented with avascular necrosis of femoral head for a period from November 2018 to June 2020 were taken in this study.

Method of collection of data

Well informed consent was taken from each patient in this study. The details of history were entered into a proforma. In patients with history of alcoholism, detailed information of the amount and duration of alcohol intake was recorded. In those on steroids, precise information was obtained about the indication, regime, dosage, and adverse event or complications. The patients were asked about smoking, lifestyle, specific family history, and associated systemic illness. Routine laboratory investigations such as complete blood count, renal function test, lipid profile and coagulation profile were performed for all patients. The patients with suspected condition or specific disease were further evaluated with specific laboratory and radiological investigations. For example- serum acid phosphatase for Gaucher's disease, serum electrophoresis for hemoglobinopathies, antiphospholipid antibody for systemic lupus erythematosus, and serum uric acid for gout. Patients without any abnormality were label as idiopathic. The patients were evaluated radiologically with anteroposterior and lateral radiographs of the hip joint and magnetic resonance imaging. Work up and lab investigation for metabolic syndrome was done. All the data was filled up in a proforma.

Waist circumference measurement- The waist circumference was measured at the midpoint between the lower margin of the last palpable ribs and the top of the iliac crest, using a stretch-resistant tape that provides as constant 100 g tension. Hip circumference was measured around the widest portion of the buttocks, with the tape parallel to the floor.

Inclusion Criteria-

- Men or women with age above 18 yrs with features of AVN irrespective of any systemic diseases.

Exclusion Criteria-

- Fractures of the acetabulum, femoral head and neck of femur.
- Dislocation of hip joint.
- Diagnosed neoplastic condition.
- Immune compromised conditions.
- Septic arthritis of hip joint.
- Osteomyelitis of proximal femur.
- Osteomyelitis of pelvis.

Outcome

This study analysed the risk factors associated with the development of avascular necrosis of the femoral head.

Statistical Analysis

Data were described in term of range, mean, standard deviation (SD), frequencies (number of cases) and relative frequencies (percentage) as appropriate. All statistical analysis were considered significant at <0.05 level of significance. The statistical data were analysed using SPSS (Statistical Package for the Social Science) 21 version statistical program for Microsoft Windows.

OBSERVATION AND RESULTS

This was a prospective study in which all patients presented to Dayanand Medical College and Hospital with a diagnosis of avascular necrosis of the femoral head between November 2018 to June 2020 were included to look for the risk factors associated with the development of AVN. The study included a total of 60 patients diagnosed with AVN.

Table 4- Mean age of total patients.

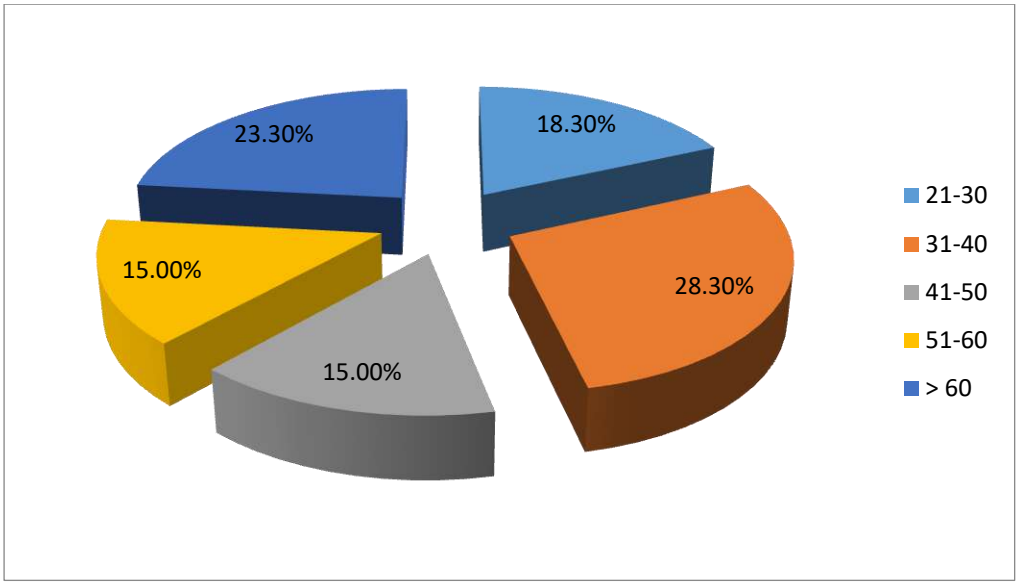
	No. of patients	Minimum	Maximum	Mean	Std. Deviation
Age	60	21.0	72.0	46.7	14.7

Mean age of patients was 46.7 years with a minimum age of 21 years and a maximum of 72 years.

Table 5- Showing age distribution.

Age group	No. of cases	Percentage
21-30	11	18.3%
31-40	17	28.3%
41-50	9	15.0%
51-60	9	15.0%
> 60	14	23.3%
Total	60	100.0%

Figure 1- Showing age distribution.

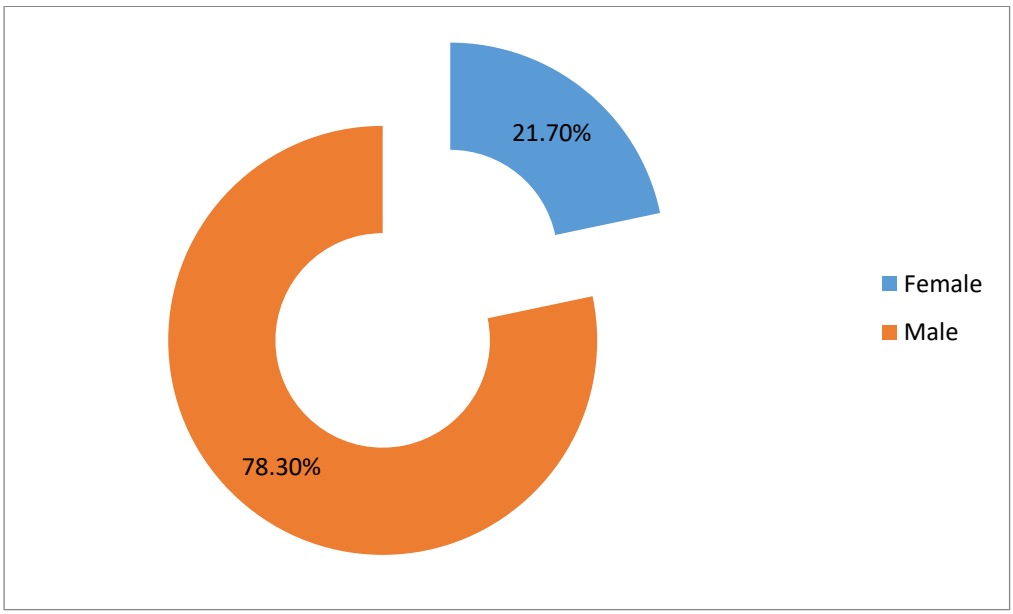


It was observed that 17 [28.3%] patients were between the age group of 31 to 40 years of age. The majority of our cases were in the 4th decade. The second peak of incidence was noted in 7th decade (14 cases: 23.3%)

Table 6- Showing sex distribution.

Gender	No. of cases	Percentage	p value
Female	13	21.7%	0.0001**
Male	47	78.3%	
Total	60	100.0%	

Figure 2- Showing sex distribution.

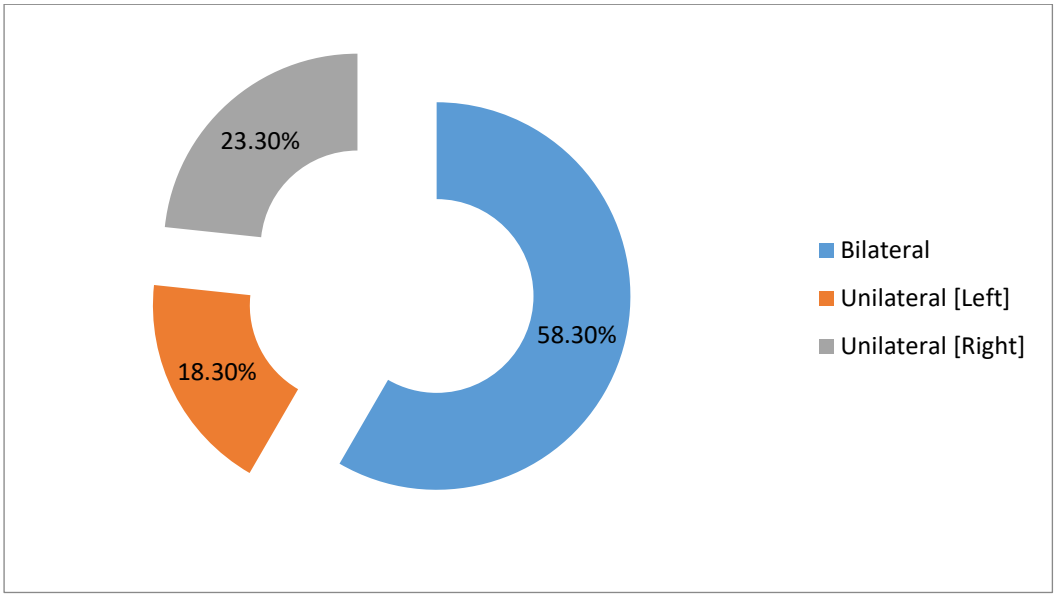


Out of the 60 patients studied, 47 patients were male constituting a little more than 3/4th of the patients.

Table 7- Distribution of patient with AVN according to side affected.

Side involvement	No. of cases	Percentage	p value
Bilateral	35	58.3%	0.0001**
Unilateral [Left]	11	18.3%	
Unilateral [Right]	14	23.3%	
Total	60	100.0%	

Figure 3- Distribution of patient with AVN according to side affected.

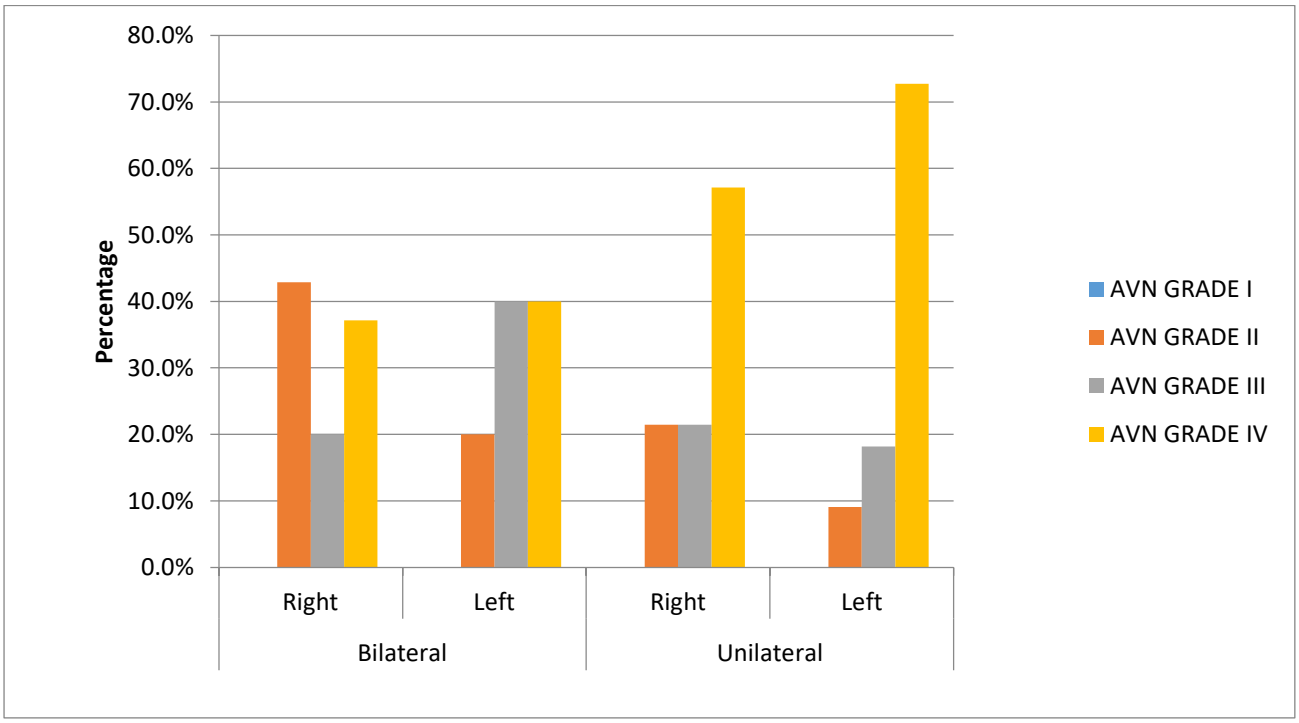


It was observed that more than half of the cases were bilateral (58.3%). Unilateral AVN were noticed in 25 patients (41.6%). Out of all 25 unilateral patients AVN right side (23.3%) was more often involved as compared to left side (18.3%).

Table 8- Showing stage of disease on the basis of Ficat and Arlet classification.

Ficat and Arlet classification	Bilateral				Unilateral				Total	
	Right		Left		Right		Left			
	N	%	N	%	N	%	N	%	N	%
AVN grade I	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%
AVN grade II	15	42.9%	7	20.0%	3	21.4%	1	9.1%	26	27.4%
AVN grade III	7	20.0%	14	40.0%	3	21.4%	2	18.2%	26	27.4%
AVN grade IV	13	37.1%	14	40.0%	8	57.1%	8	72.7%	43	45.3%
Total	35	100.0%	35	100.0%	14	100.0%	11	100.0%	95	100.0%

Figure 4- Showing stage of disease on the basis of Ficat and Arlet classification.



According to Ficat and Arlet classification, It was observed most of our patients present late with advanced disease i.e. 69 hips (71.5%) with grade III and IV. None of our patient was presented with grade I disease .

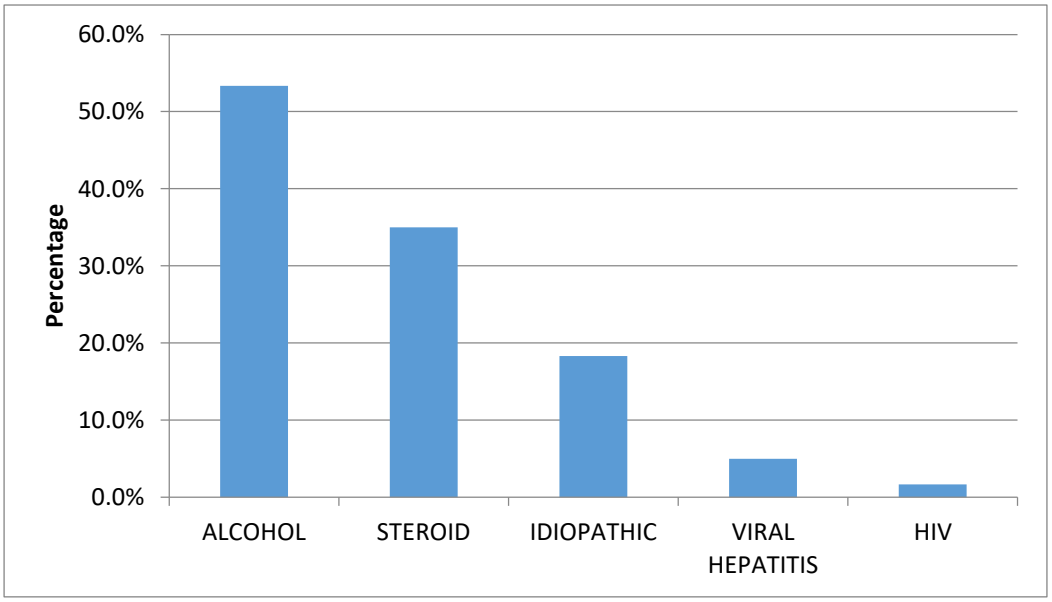
Table 9- Showing in Relation to Aetiology Distribution.

Aetiology [risk factor for AVN]	No. of cases	Percentage
Alcohol *	19+8+5=32	42.3%
Steroid**	13+8=21	35.0%
Idiopathic	11	18.3%
Viral hepatitis	3	5.0%
HIV	1	1.7%

*Dual risk factor of alcohol and steroid was found in 8 cases (13.3%) and alcohol and smoker in 5 cases (7.3%).

**Dual risk factor of steroid and alcohol was found in 8 cases (13.3%).

Figure 5- Showing in Relation to Aetiology Distribution.

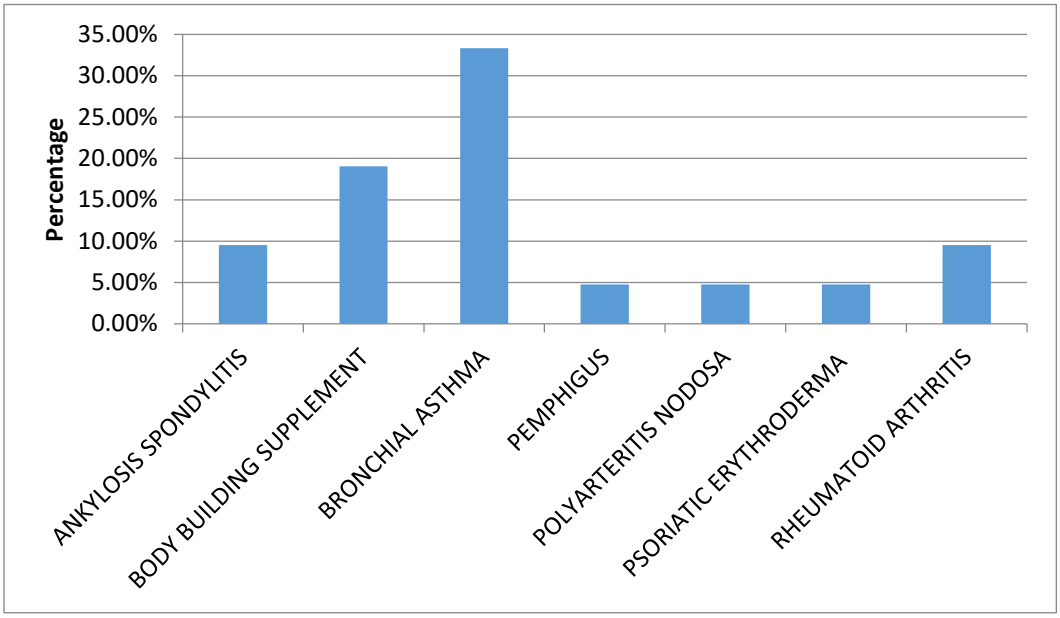


It was observed that AVN with associated alcohol intake alone was seen in 31.7% of patients. However, dual risk of alcohol drinker with history steroid intake and smoking increases its incidence upto 42.3%. Steroid was implicated in causation of AVN in 21 patients (35%). In our study 3 AVN patients (5%) had risk factor assiociated with viral hepatitis and 1 AVN patient (1.7%) with HIV. Cases in which no aetiology was found were labeled as idiopathic. In 11 patients (18.3%) because that could not be elicited.

Table 10- Showing underlying cause of Steroid administration.

Cause of Steroid administration	No. of cases	Percentage
Bronchial asthma	7	33.33%
Body building supplement	4	19.05%
SLE	3	14.29%
Ankylosis spondylitis	2	9.52%
Rheumatoid arthritis	2	9.52%
Pemphigus	1	4.76%
Polyarteritis nodosa	1	4.76%
Psoriatic erythroderma	1	4.76%
Total	21	100.00%

Figure 6- Showing underlying cause of Steroid administration.

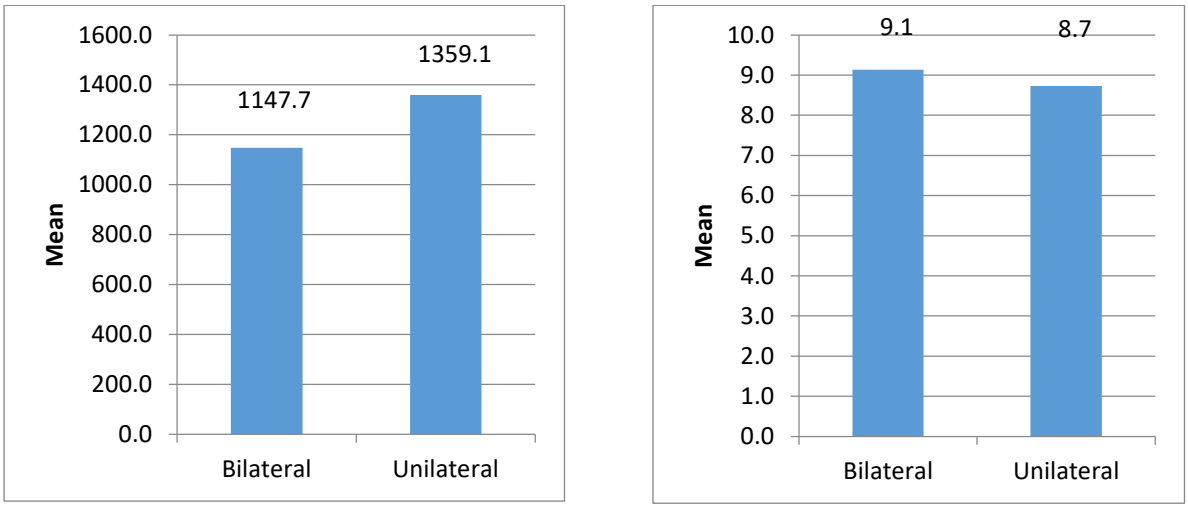


The underlying cause of steroid administration included Brochial Asthma [n=7,33.3%],Body building supplement [n=4,19.05%],SLE [n=3,14.29%], Rheumatoid Arthritis [n=2,9.5%], Ankylosis Spondylitis [n=2,9.52%], Psoriatic Erythroderma [n=1,4.7%] and Polyarteritis Nodosa [n=1,4.7%] and Pemphigus [n=1,4.7%] .

Table 11- Showing the mean alcohol consumption and mean duration of alcohol ingestion.

	Side involved	Minimum	Maximum	Mean	Std. Deviation	P value
Alcohol consumption [ml/week]	Bilateral	500	2500	1147.72	527	0.329 [NS]
	Unilateral	500	2500	1359.09	669.63	
Duration of alcohol ingestion [year]	Bilateral	3	15	9.13	3.84	0.786 [NS]
	Unilateral	5	20	8.72	4.45	

Figure 7- Showing the Mean alcohol consumption and Mean duration of alcohol ingestion.

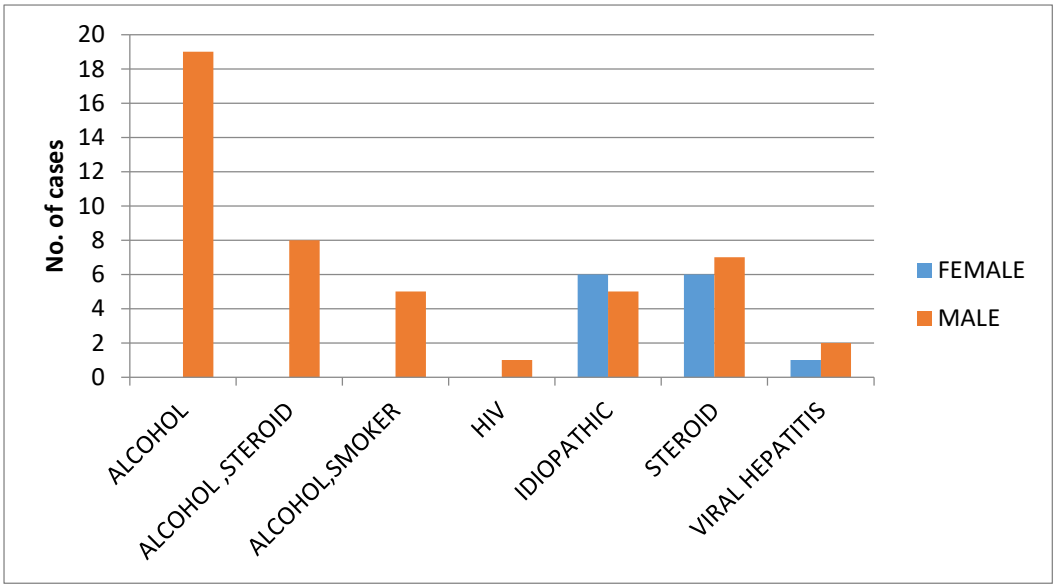


It was observed that Mean alcohol consumption in bilateral and unilateral disease was 1147 ml/week [range 500-2500 ml/week] and 1359 ml/week [range 500-2500ml/week] respectively. The Mean duration of alcohol ingestion in bilateral and unilateral disease were 9.13 years and 8.72 years respectively.

Table 12- Distributions of the AVN patients as per their sex and aetiology.

Aetiology [risk factor for AVN]	Sex	
	Female	Male
Alcohol	0	19
Alcohol, steroid	0	8
Alcohol, smoker	0	5
HIV	0	1
Idiopathic	6	5
Steroid	6	7
Viral hepatitis	1	2
Total	13	47

Figure 8- Distributions of the AVN patients as per their sex and aetiology.

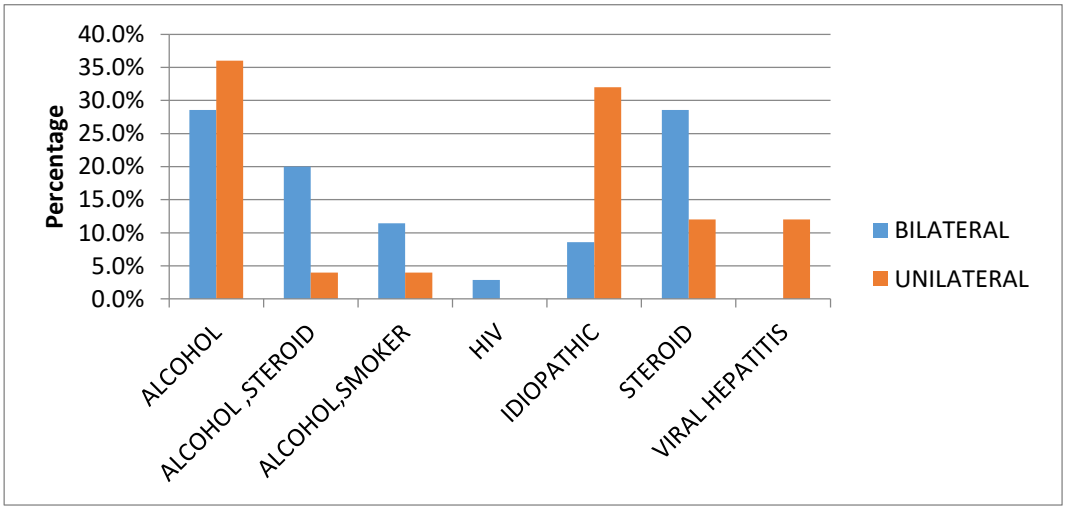


It was observed that Male predominant in alcohol group. Among total female AVN patient, half of female had history of steroid intake. There is no significant difference between male and female patients when Idiopathic, Steroid, HIV and Viral hepatitis [M:F= 2:1] risk factors were considered.

Table 13- Distributions of the AVN patients as per their side involvement and aetiology.

Aetiology [risk factor for AVN]	Side involvement				P-Value
	Bilateral		Unilateral		
	n	%	n	%	
Alcohol	10	28.6%	9	36.0%	0.541
Alcohol, steroid	7	20.0%	1	4.0%	0.072
Alcohol, smoker	4	11.4%	1	4.0%	0.305
HIV	1	2.9%	0	0.0%	0.394
Idiopathic	3	8.6%	8	32.0%	0.039* (Significant)
Steroid	10	28.6%	3	12.0%	0.124
Viral hepatitis	0	0.0%	3	12.0%	0.067
Total	35	100.0%	25	100.0%	

Figure 9- Distributions of the AVN patients as per their side involvement and aetiology.



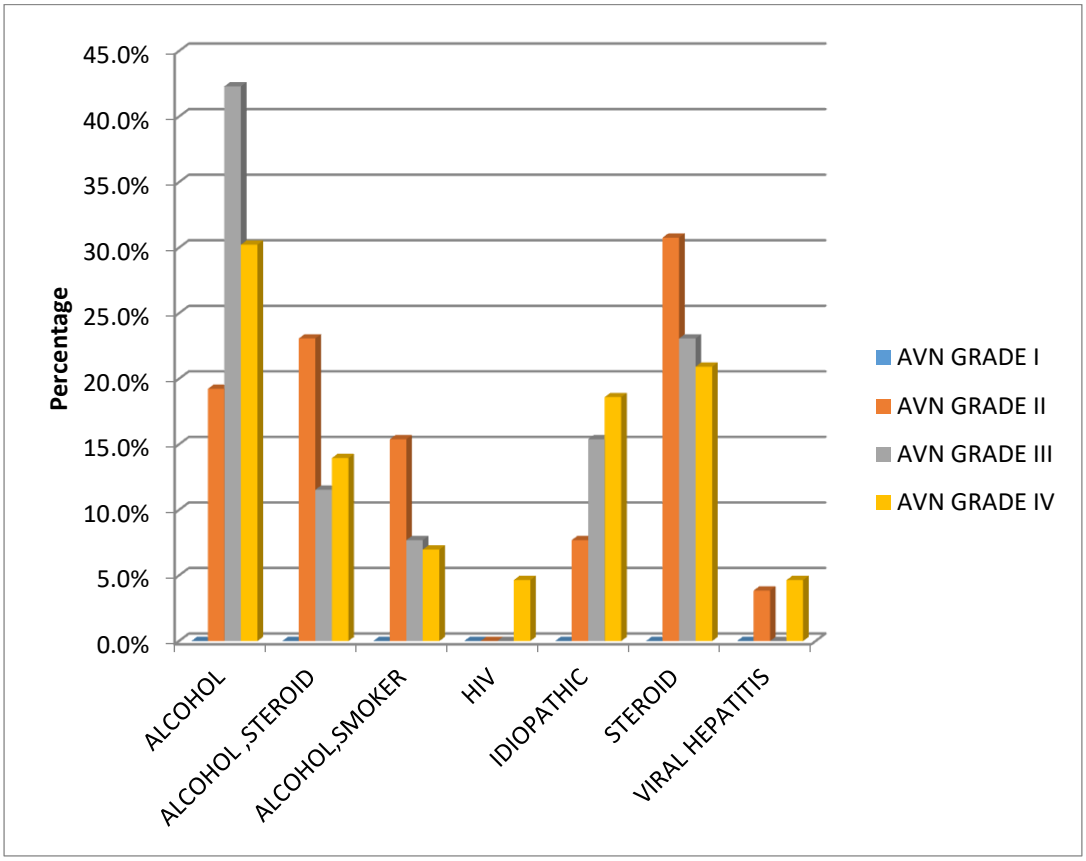
It was observed that incidence of predominantly bilateral disease seen in steroid induced AVN group (out of total 13 patients, 10 patients were bilateral), alcohol and steroid induced AVN group (out of total 8 patients, 7 patients were bilateral), alcohol and smoker induced AVN group (out of total 5 patients, 4 patients were bilateral). Whereas equal incidence of unilateral and bilateral disease was observed in alcohol

induced AVN group. In idiopathic and viral hepatitis induced AVN group incidence of unilateral disease were observed.

Table 14- Severity of the disease (Ficat and arlet classification) among patients of different etiology.

Etiology [risk factor for AVN]	Ficat and arlet classification								Total
	AVN Grade I		AVN Grade II		AVN Grade III		AVN Grade IV		
	n	%	n	%	n	%	n	%	
Alcohol	0	0.0%	5	19.2%	11	42.3%	13	30.2%	29
Alcohol, steroid	0	0.0%	6	23.1%	3	11.5%	6	14.0%	15
Alcohol, smoker	0	0.0%	4	15.4%	2	7.7%	3	7.0%	9
HIV	0	0.0%	0	0.0%	0	0.0%	2	4.7%	2
Idiopathic	0	0.0%	2	7.7%	4	15.4%	8	18.6%	14
Steroid	0	0.0%	8	30.8%	6	23.1%	9	20.9%	23
Viral hepatitis	0	0.0%	1	3.8%	0	0.0%	2	4.7%	3
Total	0	0.0%	26	100.0%	26	100.0%	43	100.0%	95

Figure 10- Severity of the disease (Ficat and arlet classification) among patients of different etiology.

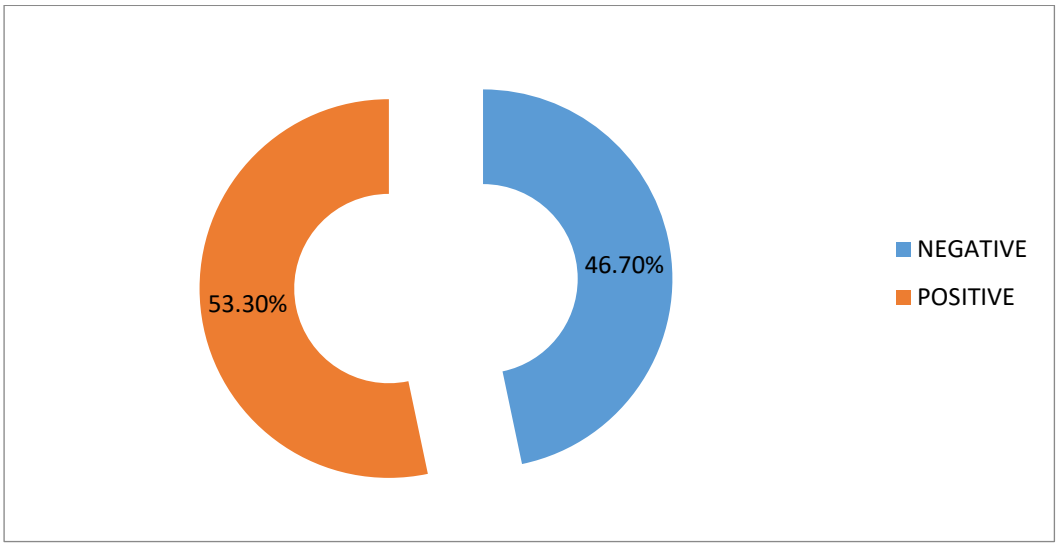


Sixty patients with 95 AVN hips were distributed as per their severity of involvement by Ficat and arlet classification. There were 45 hips in grade IV followed by 26 hips in each grade II and III. Of the total 95 hips of 60 AVN patients, alcohol induced AVN were 42.3% and 30.2% (11/13) were in grade III and IV. Accordingly, 11.5 and 14% (3/6) in alcohol and steroid group, 7.7% and 7.0% (2/3) in Alcohol and Smoker group, 23.1% and 20.9% (6/9) in Steroid induced group, 0% and 4.7% (0/2) in HIV, 0% and 4.7% (0/2) in Viral hepatitis group and 15.4% and 18.6% (4/8) in Idiopathic group were in grade III and IV respectively. No patient was noticed in grade I in any etiology.

Table 15- Distribution of number of cases in the study groups based on the metabolic syndrome.

Metabolic profile acc to IDF classification	No. of cases	Percentage	P value
Negative	28	46.7%	0.606 [NS]
Positive	32	53.3%	
Total	60	100.0%	

Figure 11- Distribution of number of cases in the study groups based on the metabolic syndrome.

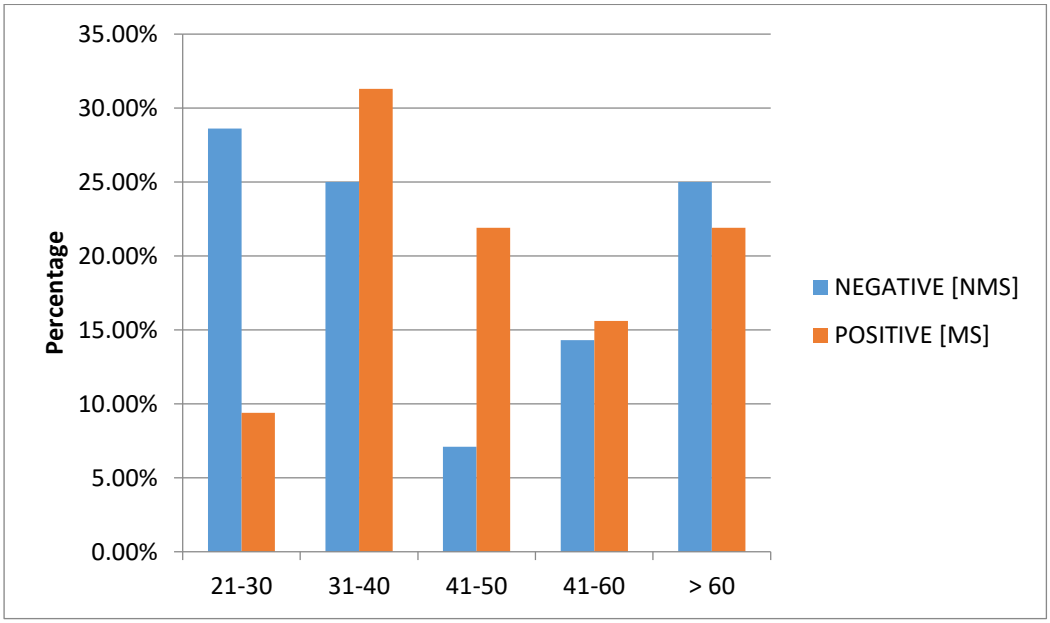


Among 60 patients studied, the prevalence of metabolic syndrome was 53.3%.

Table 16- Distribution of age in the study groups based on the metabolic syndrome.

Age group	NMS group (only AVN)		MS group (AVN with metabolic syndrome)		Total	P-value
	N	%	N	%		
21-30	8	28.6%	3	9.4%	11	0.244 [NS]
31-40	7	25.0%	10	31.3%	17	
41-50	2	7.1%	7	21.9%	9	
41-60	4	14.3%	5	15.6%	9	
> 60	7	25.0%	7	21.9%	14	
Total	28	100.0%	32	100.0%	60	

Figure 12- Distribution of age in the study groups based on the metabolic syndrome.

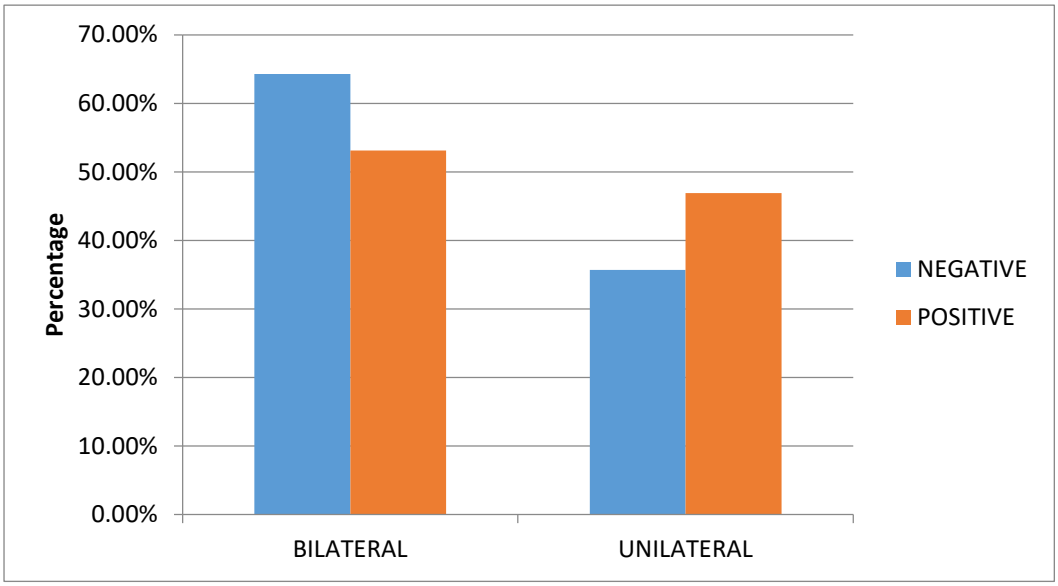


Data are expressed as absolute numbers with percentage. NMS = Patients with AVN only. MS= Patients with AVN and Metabolic syndrome.

Table 17- Distribution of side involved in the study groups based on the metabolic syndrome.

Side involved	NMS group (only AVN)		MS group (AVN with metabolic syndrome)		Total	P-value
	N	%	N	%		
Bilateral	18	64.3%	17	53.1%	35	0.382 [NS]
Unilateral	10	35.7%	15	46.9%	25	
Total	28	100.0%	32	100.0%	60	

Figure 13- Distribution of side involved in the study groups based on the metabolic syndrome.

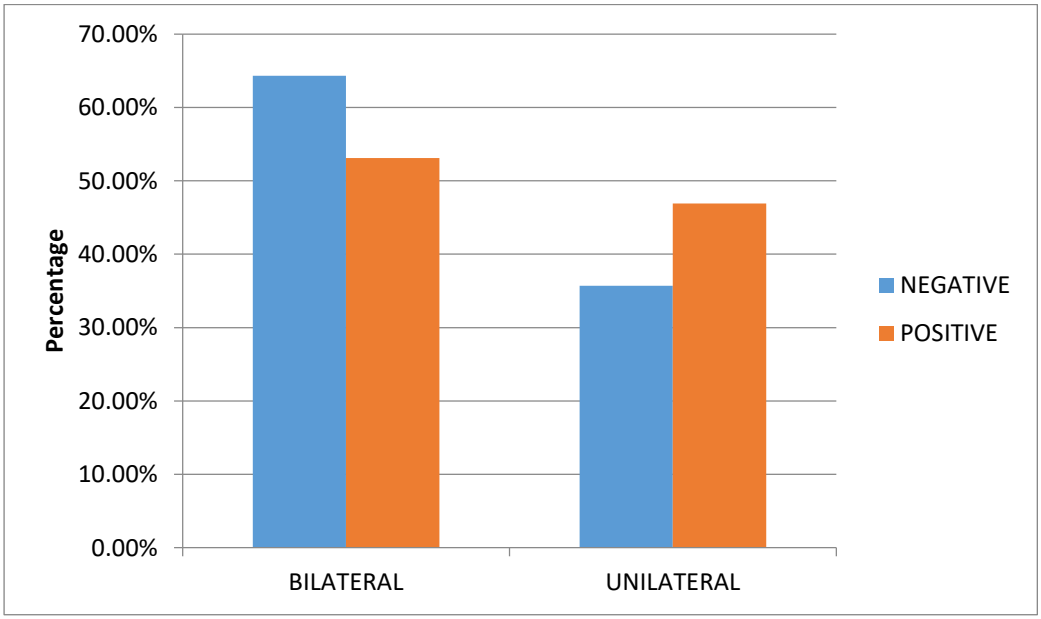


Data are expressed as absolute numbers with percentage.

Table 18- Distribution of sex in the study groups based on the metabolic syndrome.

Gender	Metabolic profile acc. to IDF classification				Total	P-value
		Negative		Positive		
Female	9	32.10%	4	12.50%	13	0.065
Male	19	67.90%	28	87.50%	47	
Total	28	100.00%	32	100.00%	60	

Figure 14- Distribution of sex in the study groups based on the metabolic syndrome.

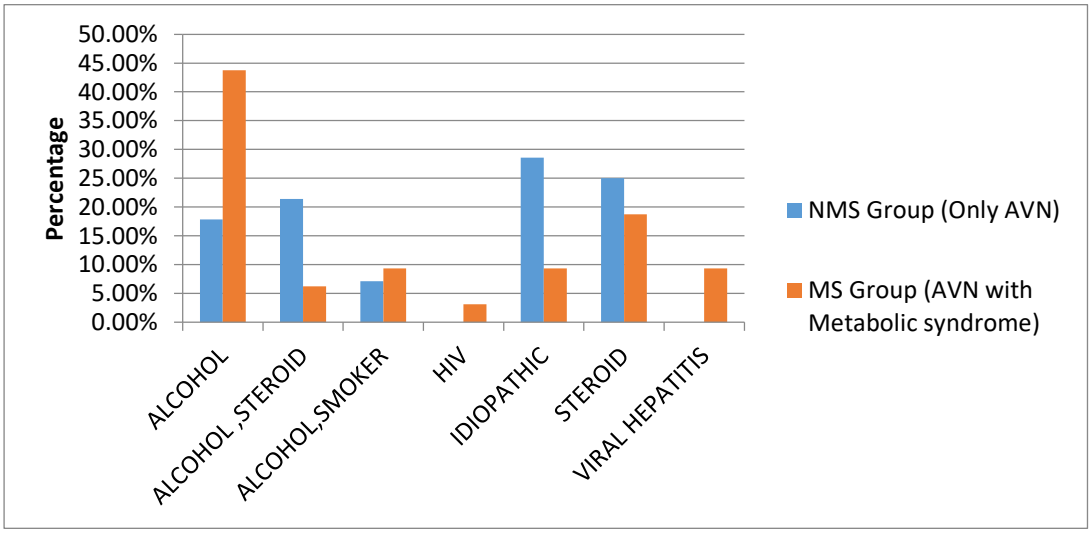


Data are expressed as absolute numbers and percentage. It was tested to be marginally statistically significant.

Table 19- Distribution of etiology in the study groups based on the metabolic syndrome.

Etiology [risk factor for AVN]	NMS group (only AVN)		MS group (AVN with metabolic syndrome)		Total
	N	%	N	%	
Alcohol	5	17.86%	14	43.75%	19
Alcohol, Steroid	6	21.43%	2	6.25%	8
Alcohol, Smoker	2	7.14%	3	9.38%	5
HIV	0	0.00%	1	3.13%	1
Idiopathic	8	28.57%	3	9.38%	11
Steroid	7	25.00%	6	18.75%	13
Viral hepatitis	0	0.00%	3	9.38%	3
Total	28	100.00%	32	100.00%	60

Figure 15- Distribution of etiology in the study groups based on the metabolic syndrome.

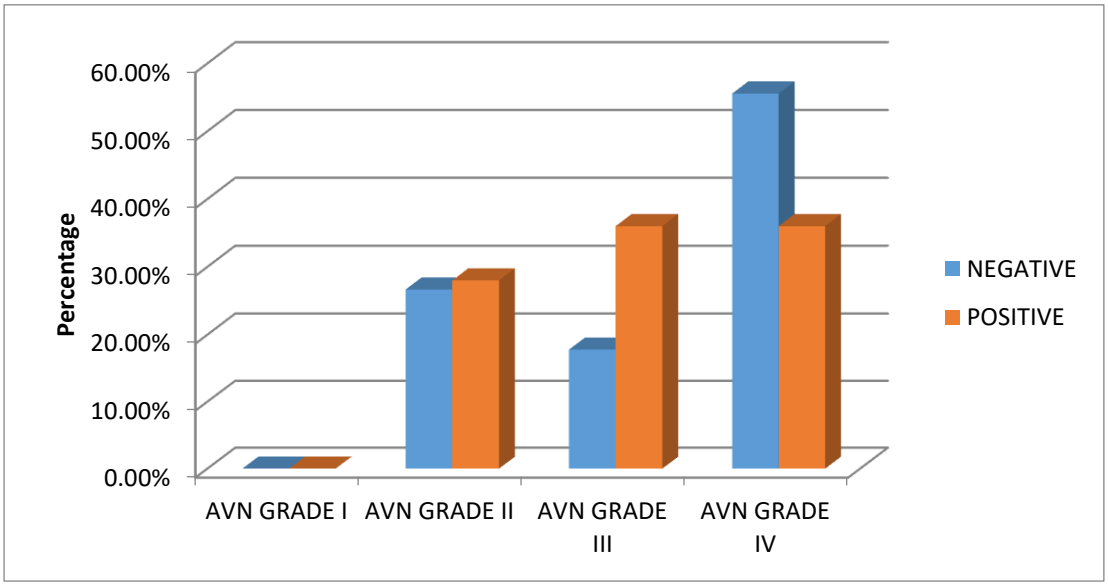


In MS group of patients, alcohol induced AVN was 43.75% followed by steroid induced AVN 18.75% and idiopathic cause of AVN 9.38%. In NMS group, Idiopathic cause of AVN was 28.57% followed by steroid induced AVN 25% and both alcohol and steroid induced AVN was 21.43%.

Table 20- Distribution of stage of disease in the study groups based on the metabolic syndrome.

Ficat and arlet classification	NMS group (only AVN)		MS group (AVN with metabolic syndrome)		Total	P-value
	N	%	N	%		
AVN grade I	0	0.00%	0	0.00%	0	0.086[NS]
AVN grade II	12	26.67%	14	28.00%	26	
AVN grade III	8	17.78%	18	36.00%	26	
AVN grade IV	25	55.56%	18	36.00%	43	
Total	45	100.00%	50	100.00%	95	

Figure 16- Distribution of stage of disease in the study groups based on the metabolic syndrome.



Data are expressed as absolute numbers with percentage.

Table 21- Comparison of parameters of the metabolic syndrome components.

	N	Minimum	Maximum	Mean	Std. Deviation
Waist circumference	60	63.0	125.0	99.3	9.8
Triglyceride	60	41.0	830.0	189.7	111.1
HDL cholesterol	60	15.0	60.0	40.4	9.8
Blood pressure (SBP)	60	59.0	299.0	143.6	39.4
Blood pressure (DBP)	60	21.0	90.0	66.1	22.5
Fasting plasma glucose	60	79.0	177.0	97.9	14.9

Figure 17- Comparison of parameters of the metabolic syndrome components.

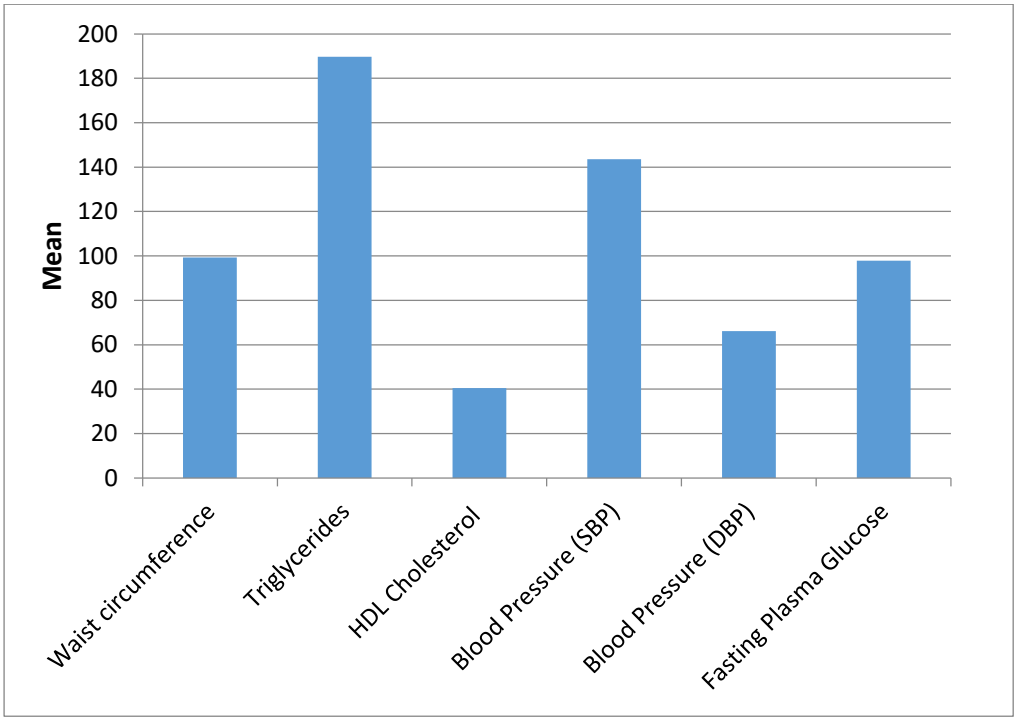
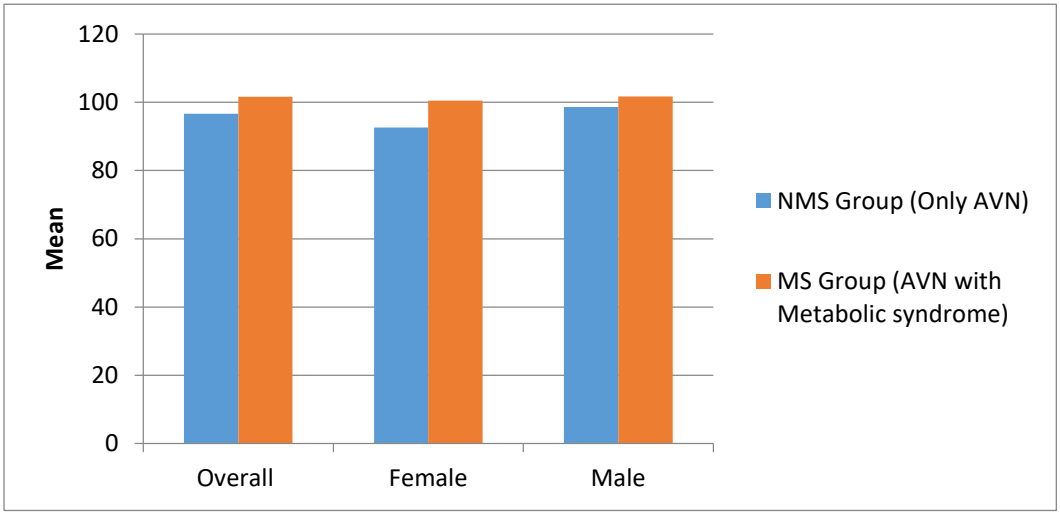


Table 22- Comparison of waist circumference between the groups in the study population.

Waist circumference	NMS group (only AVN)		MS group (AVN with metabolic syndrome)		T	P-value
	Mean	SD	Mean	SD		
Overall	96.64	10.65	101.56	8.49	-1.989	0.05*
Female	92.56	6.42	100.50	10.12	-1.737	0.110
Male	98.58	11.81	101.71	8.44	-1.063	0.294

Figure 18- Comparison of waist circumference between the groups in the study population.



Data are expressed as absolute numbers and percentage. * indicates P value <0.05 which is considered highly significant.

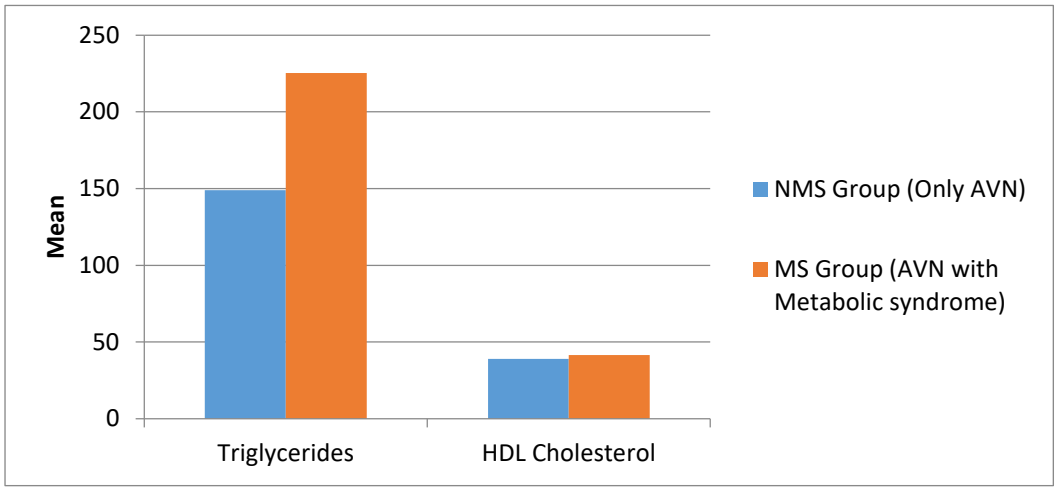
Table 23- Comparison of biochemical parameters between the groups in the study population.

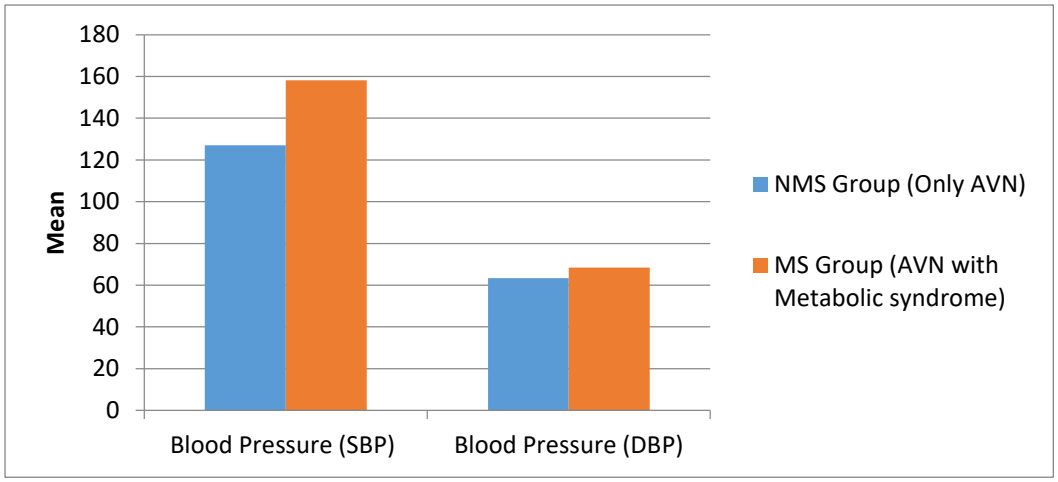
	NMS group (only AVN)		MS group (AVN with metabolic syndrome)		T	P-value
	Mean	SD	Mean	SD		
Triglyceride	149.04	75.81	225.25	125.31	-2.799	0.007*
HDL Cholesterol	39.07	11.21	41.50	8.50	-0.952	0.345

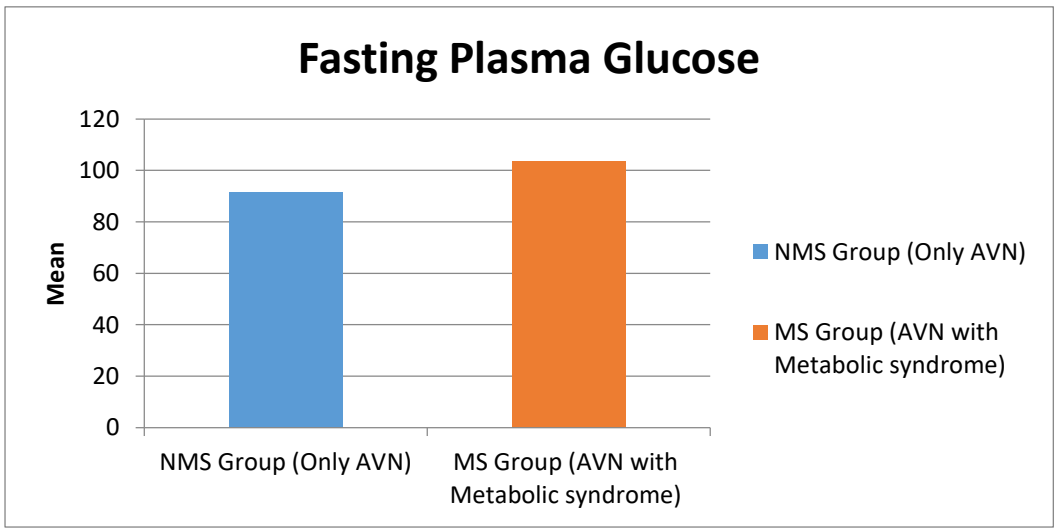
	NMS group (only AVN)		MS group (AVN with metabolic syndrome)		T	P-value
	Mean	SD	Mean	SD		
Blood pressure (SBP)	127.04	32.48	158.13	39.64	-3.293	0.002*
Blood pressure (DBP)	63.43	20.22	68.44	24.33	-0.860	0.393

	NMS group (only AVN)		MS group (AVN with metabolic syndrome)		T	P-value
	Mean	SD	Mean	SD		
Fasting plasma glucose	91.57	5.41	103.38	18.09	-3.321	0.002*

Figure 19- Comparison of biochemical parameters between the groups in the study population.





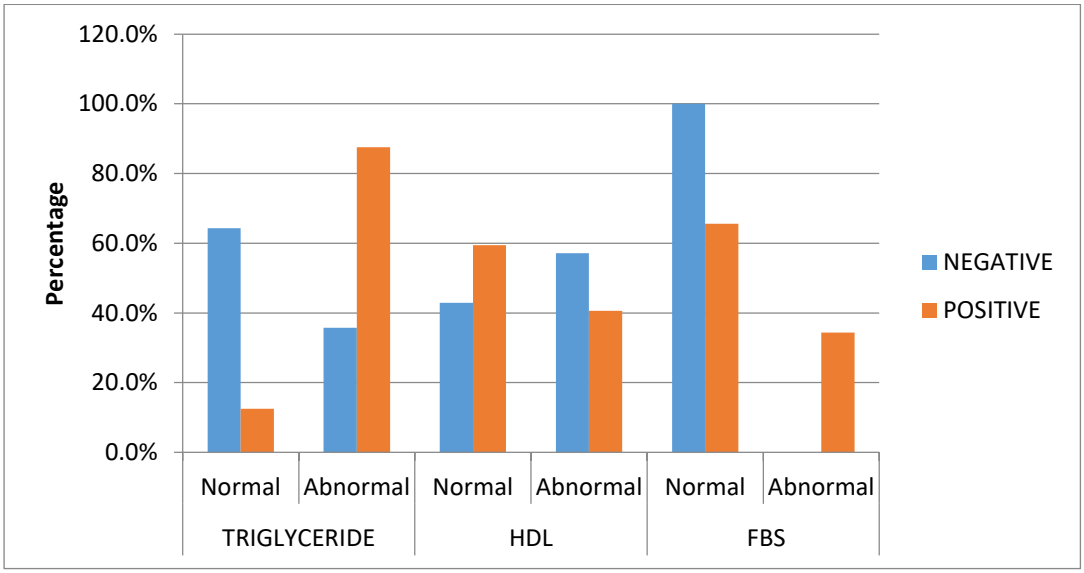


Data are expressed as mean with standard deviation. * indicates P value <0.05 which is considered highly significant.

Table 24- Comparison of biochemical components of metabolic syndrome between the groups in the study population.

		NMS group (only AVN)		MS group (AVN with metabolic syndrome)		Total	P-value
		N	%	N	%		
Triglyceride	Normal	18	64.3%	4	12.5%	22	0.0001**
	Abnormal	10	35.7%	28	87.5%	38	
		28	100.0%	32	100.0%	60	
HDL	Normal	12	42.9%	19	59.4%	31	0.201
	Abnormal	16	57.1%	13	40.6%	29	
		28	100.0%	32	100.0%	60	
FBS	Normal	28	100.0%	21	65.6%	49	0.001*
	Abnormal	0	0.0%	11	34.4%	11	
Total		28	100.0%	32	100.0%	60	

Figure 20- Comparison of biochemical components of metabolic syndrome between the groups in the study population.

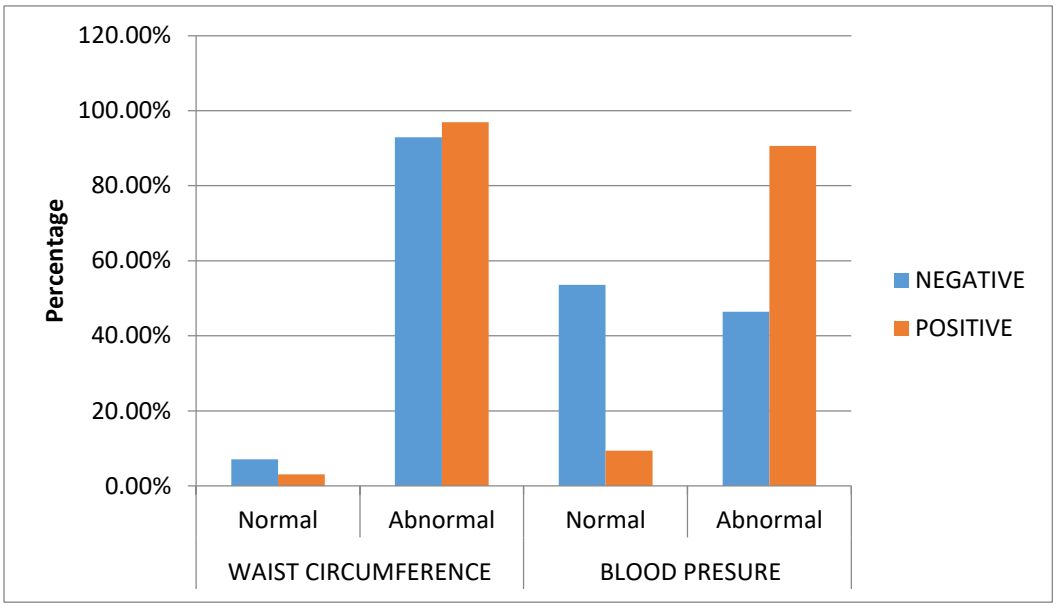


Data are expressed as absolute numbers and percentage. * indicates P value <0.05 which is considered highly significant. ** indicates P value <0.0001 which is considered extremely significant.

Table 25- Comparison of clinical components of metabolic syndrome between the groups in the study population.

		NMS group (only AVN)		MS group (AVN with metabolic syndrome)		Total	P-value
		N	%	N	%		
Waist circumference	Normal	2	7.1%	1	3.1%	3	0.476
	Abnormal	26	92.9%	31	96.9%	57	
		28	100.0%	32	100.0%	60	
Blood pressure	Normal	15	53.6%	3	9.4%	18	0.0001**
	Abnormal	13	46.4%	29	90.6%	42	
Total		28	100.0%	32	100.0%	60	

Figure 21- Comparison of clinical components of metabolic syndrome between the groups in the study population.



Data are expressed as absolute numbers and percentage. ** indicates P value <0.0001 which is considered extremely significant.

DISCUSSION

Femoral head avascular necrosis remains as an intractable disease, and medical efforts regarding AVN have mainly focused on treatment rather than prevention. Over a period of time a lot of etiological factors have been implicated to cause AVN of femoral head. Literature is lacking on prevalence of various known risk factors for AVN from India. AVN leads to significant disability in the most productive years of life and is one of the common causes of hip arthroplasty in younger individuals. Knowing the frequency of causative factors might be useful for developing preventive measures.

Age- Information regarding age distribution would help to establish appropriate treatment strategies for different age groups. In our study, mean age of patients enrolled in our study was 46.7 years. Sugano et al[48] and Wang et al [24] from China and Kang et al[23] from Korea studied the mean age of patients presenting with AVN was about 44years, 48 years and 50 years respectively. So our observations are comparable with other studies from Asian region.

Dun and Grow[49], Bukley et al [50] and Vardhan et al in their studies reported mean age of AVN was 41.5 years, 40 years and 30 years respectively which are not in concordance to our study. However Cooper et al[26] from the UK reported the mean age to be slightly higher i.e. 57.6 years in their patients.

Fukushima et al[25] from Japan and Wang et al[24] reported that AVN was seen commonly in their 40s. In our study, majority of their patients are in 4^{th} decade. It seems the disease is quite prevalent in the young individuals during their active period of life.

Sex distribution- Our study had 78.3% male patients The studies from Fukushima et al[25], Kang et al[23], Wang et al[24] and Cooper et al[26] reported 58.28%, 77.76%, 73.91%, and 47% male patients suffering from AVN. Our results are comparable with Kang et al and Wang et al studies. However, it is quite evident that in Asian subcontinent, male patients are more commonly affected than females[23,24,49]. In case of female predominantly [more than half] the cause of AVN is steroid

intake and none of females had history of alcohol consumption probably due to social norms. In our study, bilateral involvement of the hip was observed in 58.3% cases. Sugano et al[48] and Vardhan et al[31] reported 67% and 61.6% bilateral AVN cases which are comparable to our study. Kang et al[23] from Korea found that 37% of their patients presented with bilateral disease. This discrepancy was due to non-inclusion of the asymptomatic contralateral hip by Kang et al[23].

Smoking- De Bastiani el al found that smoking is strongly associated with AVN patients. Cigarette smokers were defined as those who smoked at least one cigarette per day. In our study, history of smoking were found in 7.3% of patient. Smoking is not prevalent in the population served by our hospital due to religious and social norms. Therefore, incidence was less and no meaningful conclusion could be drawn.

Idiopathic- In the current study, 18.3% patients were idiopathic, where there was no identifiable risk factor observed. In the study of Fukushima et al[25], idiopathic AVN accounted for 15% of total cases. Thus, there is small difference in the distribution of this etiological profile.

Alcoholism- In our study, AVN associated with alcohol intake alone was seen in 31.7% of patients. However, alcohol intake with history of steroid intake and/or smoker increases its incidence upto 42.3%. The mean alcohol intake in patients with unilateral involvement was 1359 ml/week and in patients with bilateral involvement the mean intake was about 1147 ml/week. The mean duration of intake of alcohol in unilaterally affected patients was 9 years and in patients with bilaterally involved patients, the mean duration was about 8 years. Though there is difference, but it shows to be statistically non-significant.

In 1962, Massias et al[51] confirmed etiologic role of alcohol in AVN. Frequency varied from 10% to 42%. In the study of Fukushima et al[25] and Kang et al[23] the habitual use of alcohol accounted for 31% and 32.4% respectively. In our study, alcoholism alone was associated with little over third of total AVN cases. However, other authors have also shown in their study about 1/3rd cases are habitual users of alcohol. Thus, there is smaller difference in the etiologic profile secondary to alcohol intake. The proportion of alcohol induced AVN in our study is

comparable to the above mentioned Massias et al, Fukushima et al and Kang et al studies. In the present study, all patients with AVN secondary to alcohol intake were males. This is because of the well accepted social characteristics of Indian culture where alcohol intake is not common among females.

Alcohol intake is the important factor contributing to AVN. Although individual sensitivity to alcohol also appears to be an important factor for AVN development, alcohol has been known as an independent risk factor, when taken in excess [27,28].

Table 26- Showing the percentage of alcohol induced AVN cases in different studies.

Author	Frequency
Massias et al (1962)[51]	10-42%
Patterson et al (1964)[52]	17%
Sugioka et.al (1976).[28]	2%
Serre and Simon[51]	19%
Japanese orthopedic surgeons committee (1988)	21.80%
Fukushima et al[25]	31%
Kang et al.[23]	32.4 %
Our study	31.7%

In our study, the different pattern of correlation between alcohol intake and AVN were noticed which results from the variability of underlying additional risk factors like smoking and steroid use. Steroid use and smoking can be a critical confounding factor when evaluating the effect of alcohol intake for AVN. In our study 8 patients (13.3%) were related with both alcohol and steroid and 5 patients (7.3%) with related with both alcohol and smoker. Fukushima et al[25] investigated the possible interactions between alcohol intake and oral corticosteroid use . However, when combined effect of alcohol and steroids was observed, the added effect of alcohol intake was found to make significant

difference in the presence of the overwhelming effect of steroids in the development of AVN.

Steroid- In our study 35% of AVN of femoral head was due to steroid intake [21.7% steroid alone and 13.3% in addition with alcohol intake].

In 1988 Committee survey by Japanese Orthopedic Surgeons estimated the AVN of femoral head occurred in 2500-3300 adults during 1988 alone. Of these cases, 34.7% were due to steroid. In the study of vardhan et al**[31],** steroid induced AVN accounted for 37.3% in Indian population. Our results are comparable with these results. Thus, there is smaller difference in this profile. In the study of Kang et al[23] have shown half of incidence [14.6%] as in our study. In the study from France[22] where 30% AVN were secondary to steroid intake. However studies from France[22] have shown similar risk of AVN with steroid intake.

Recently using unauthorized drugs in bodybuilding specially steroids has become a new concern that may incite femoral head AVN[53]. The study by Javad mortazavi at et[54] in 2019 shown bodybuilding supplement is the risk factors for AVN of femoral head in athletes . In our study, 4 young male patients diagnosed with AVN disease had past history of taking bodybuilding supplement and steroid in the form of powder and injection form. There is a need for comprehensive studies to demonstrate effects of bodybuilding supplement on bone and vascularity metabolism. In the future it is crucial that the reveal etiology for the more cost effective and more functional therapies.

Viral infection- Recent retrospective case studies of HIV patients have reported incidences ranging from 0.03 to 0.37 cases per 100 person-years. Yeghaneh et al[55] studied the prevalence of femoral head AVN is almost 0.45% among HIV patients which is approximately 45 times more than the rest of Society. AVN occurs 0.088%-1.33% annually among HIV victims. This study observed that the prevalence of HCV, HBV, and HIV was 1.7%, 1.1%, and 1.1% respectively. In our study, 1.7%, 1.66%, 3.3% AVN patients were detected to be HIV, HCV and HBV positive respectively. Thus, there is smaller difference in this profile.

Infection with HIV, HBV and HCV will increase the risk of avascular bone necrosis. Currently the rate of these infections is accelerating in Community. The earlier diagnosis through screening can result in a better prognosis for the patients. On population basis, HCV has high incidence in our region. Therefore, it may be pertinent to screen the HCV patient for AVN.

Metabolic syndrome- The prevalence of metabolic syndrome with IDF-criteria was 53.3% (87.5% male and 12.5% female) in our study. The most predominant component of metabolic syndrome abnormality among the AVN patients was high blood pressure. More than 50% of patients found between 31 to 50 years age group. Regarding the involvement of side, sex, severity of AVN disease, there were no significant association found with metabolic syndrome. In our study, out of 60 AVN diagnosed patients, the 32 patients had metabolic syndrome based on IDF criteria. These 32 patients were taken as study subjects and the remaining 28 patients who had no metabolic syndrome served as the control group. In metabolic syndrome group, alcohol induced AVN cases were 43.75% followed by Steroid 18.75%. Comparision of biochemical and clinical components of metabolic syndrome was done. Mean and standard deviation of triglycerides, blood pressure, waist circumference and fasting glucose parameters was tested to be statistically significant in AVN patients with metabolic syndrome and without metabolic syndrome.

Hypertension is identified as an independent risk factor and, in combination with insulin resistance, will have a synergistic effect which results in a grave risk for severe vascular events[56].

In our study, Blood pressure was elevated in 90.6% of AVN patients with metabolic syndrome, whereas only 46% of AVN patients without metabolic syndrome had abnormal blood pressure. This was tested to be statistically significant.

Abdominal/central obesity is associated with high amount of visceral fat, which is metabolically active, producing free fatty acids and inflammatory cytokines that drain directly into the liver via the portal circulation. This could elicit various complex injurious mechanisms

leading to atherosclerosis and microvascular disease[57,58]. In our study, waist circumference of more than 90 cms in male and > 80 cms in female was prevalent in 96.6% of AVN patients with metabolic syndrome. We compared both groups of patients and observed that this parameter to be non-significant statistical.

In general, overweight and obesity are often associated with hyperlipidemia. This in turn is associated with elevated fasting and postprandial plasma insulin concentrations that can promote adipose synthesis and inhibit the decomposition of adipose tissue. In our study, fasting glucose was abnormal in 34.4% of AVN patients with metabolic syndrome. This was tested to be statistically significant when compared with AVN patients without metabolic syndrome.

Dyslipidaemia has been commonly demonstrated in subjects with metabolic syndrome[58]. In our study, triglyceride was observed in 87.5% of AVN patients with metabolic syndrome, whereas only 35% of AVN patients without metabolic syndrome had abnormal blood pressure. This was tested to be statistically significant. HDL level was abnormal in 40.6% of AVN patients with metabolic syndrome, whereas only 57% of AVN patients without metabolic syndrome had abnormal blood pressure. This was tested to be statistically non-significant.

Our findings support the hypothesis that the factors involved in the pathogenesis of atherosclerotic cardiovascular disease could also contribute to the progression of AVN of femoral head. In our opinion, detecting the presence of metabolic syndrome, it may be possible to prevent the early precipitation of several disease in a community. This may help to establish basic guidelines of cure and prevention. It will be best approach to formulate a health policy at a community level to provide health care and also educate the medical graduates to understand the basic health needs of the community they serve.

This study has several limitations. AVN can be influenced by many variables other than steroid use, such as underlying diseases, the use of anticoagulants, flushing pattern, history of liver diseases and occupation. Cut-off values for alcohol consumption and steroid exposure in causing AVN have not been studied in our study. Since

social consumption of alcohol is otherwise common in most cultures world-wide, a definition of heavy alcohol use in occurrence of AVN has to be studied. We took a mean alcohol intake and mean duration in patients with unilateral and bilateral involvement. But It was statistically non-significant. Type of different alcohol (vodka, wine and beer) were not evaluated in our study. Future studies should focus on the cut-off value of alcohol consumption to prevent alcohol induced AVN. There is a need of long-term studies on patients with AVN focusing on natural history of the disease and survival analysis with THR as end point. Differences in incidence, risk factors and outcomes of AVN in different populations also points towards possibility of genetic differences or specific environmental exposures.

In the 21st century where everyone wants to succeed in life and investigate better. There is a competition among each and every one and no one wants to wait, they want instant results without doing hard work. Anabolic steroids and bodybuilding supplement are such sources which will increase your body mass and muscle mass in short period of time. Young generation is blindly following this trend without even knowing its consequences. So, by this study we want to make aware our young generation about this and its deadliest consequences.

SUMMARY

- The mean age was 46.7 years (range 21-72 years) and 46.6% (*n*=27) patients were between 21 and 40 years.
- Male to female ratio was 4:1.
- Bilateral AVN was observed in 58.3% cases.
- Alcohol consumption 42.3% was most commonly observed in the patients followed by Steroid administration in 35% patients and idiopathic in 18.3% patients.
- Among patients with a history of systemic steroid administration, Brochial asthma was reported most frequently (33.3%) as the underlying disease.
- According to Ficat and Arlet classification, there were 69 hips (71.5%) with grade III and IV. None of our patient was presented with grade I disease.
- The prevalence of metabolic syndrome was 53.3%

CONCLUSION

AVN in the Indian patients is a disease of young individuals with male predominance. There are various conditions than can be incriminated as triggers for this disease. Alcoholism and corticosteroid use account for the bulk of cases. The steroid induced AVN are usually bilateral, whereas Alcohol induced AVN has equal incidence of unilateral and bilateral involvement. In Idiopathic AVN, incidence of unilateral disease was observed.

Initially, patients are asymptomatic but with time AVN leads to joint destruction, requiring surgical treatment. It is essential that AVN of the femoral head is diagnosed early because delaying this disease by joint preserving measures has a much better prognosis and because the results of joint replacement are poorer in young individuals. Treatment has been facilitated by using widely accepted international classification systems and by effective earlier diagnosis using MRI.

An array of consistently associated systemic disorders appears to be largely linked by frequent lipid elevations. The prevalence of metabolic syndrome was 53.3% in this study. Although the pathophysiologic mechanisms of AVN are inconclusive, growing evidence has supported that several risk factors contribute to the initiation and progression of AVN process. During the past several decades, the general population has experienced remarkable changes in lifestyle as economic development and the ageing process went on. As a consequence, a variety of health problems emerged, such as the increase of the risk factor of Metabolic syndrome.

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Sr. No	MRD No	Initials	Age	Gender	Date of Admission	Joint Side	Viral Marker	Alcohol Consuption	Steroid Use/Abuse	Smoker	Metabolic profile	Waist circumference [Normal = male less than 90 and female less than 80]	Triglyceride [Normal = less than150]	HDL Cholesterol [Normal = more than 40]
1	407605	KS	38	MALE	24/11/2018	BILATERAL	NR	YES [1000ML/WEEK X 10YEARS]	NO	NO	POSITIVE	106	198	47
2	743993	PS	36	FEMALE	10/6/2019	BILATERAL	NR	NO	YES [psoriatic erythroderma]	NO	NEGATIVE	87	146	60
3	529903	PKS	36	MALE	6/8/2019	UNILATERAL [RIGHT]	NR	YES [750ML/WEEK X 5YEARS]	NO	NO	POSITIVE	92	830	33
4	765325	HD	60	FEMALE	15/7/2019	BILATERAL	NR	NO	NO	NO	NEGATIVE	92	128	57
5	780473	GS	40	MALE	5/8/2019	BILATERAL	NR	YES [2000ML/WEEK X 10YEARS]	NO	NO	POSITIVE	125	291	59
6	824534	RPS	53	MALE	6/10/2019	BILATERAL	NR	YES [1000ML/WEEK X 15YEARS]	NO	NO	POSITIVE	98	291	39
7	829853	SK	21	MALE	15/10/2019	BILATERAL	NR	YES [500ML/WEEK X 3YEARS]	YES [BODY BUILDING SUPPLEMENT]	NO	NEGATIVE	63	159	35
8	833190	J	29	FEMALE	4/11/2019	BILATERAL	NR	NO	YES [SLE]	NO	NEGATIVE	87	41	50
9	858575	KD	72	FEMALE	30/11/2019	UNILATERAL [LEFT]	NR	NO	NO	NO	NEGATIVE	85	162	38
10	857249	PS	39	MALE	27/11/2019	BILATERAL	NR	YES [1000ML/WEEK X 15YEARS]	NO	NO	POSITIVE	103	187	45
11	849692	SK	45	MALE	15/11/2019	UNILATERAL [LEFT]	NR	NO	YES [BRONCHIAL ASTHMA]	NO	POSITIVE	97	163	44
12	862534	HK	42	MALE	6/12/2019	BILATERAL	NR	YES [500ML/WEEK X 10YEARS]	YES [BODY BUILDING SUPPLEMENT]	NO	NEGATIVE	107	458	46
13	447492	HK	66	FEMALE	27/12/2019	UNILATERAL [RIGHT]	HCV	NO	NO	NO	POSITIVE	112	125	37
14	871040	PD	64	MALE	23/12/2019	BILATERAL	NR	YES [1000ML/WEEK X 10YEARS]	NO	NO	NEGATIVE	114	191	45
15	867373	RB	30	MALE	16/12/2019	BILATERAL	NR	YES [500ML/WEEK X 5YEARS]	NO	YES	POSITIVE	105	176	42
16	598447	LM	60	MALE	11/12/2019	BILATERAL	NR	YES [1000ML/WEEK X 10YEARS]	NO	YES	POSITIVE	77	232	41
17	866838	NK	29	FEMALE	14/12/2019	BILATERAL	NR	NO	YES [SLE]	NO	NEGATIVE	87	160	40
18	670797	AKG	32	MALE	11/9/2019	BILATERAL	NR	YES [1000ML/WEEK X 6YEARS]	YES [BODY BUILDING SUPPLEMENT]	NO	NEGATIVE	95	197	23
19	803631	KS	70	MALE	10/9/2019	UNILATERAL [LEFT]	NR	YES [1500ML/WEEK X 10YEARS]	NO	NO	NEGATIVE	100	143	26
20	594442	SR	49	FEMALE	10/10/2018	UNILATERAL [RIGHT]	NR	NO	NO	NO	NEGATIVE	98	139	31
21	678133	GS	70	MALE	25/2/2019	BILATERAL	NR	NO	YES [R.A.]	NO	NEGATIVE	108	121	29
22	585467	MK	36	FEMALE	4/10/2018	UNILATERAL [RIGHT]	NR	NO	YES [POLYARTERITIS NODOSA]	NO	NEGATIVE	100	69	35
23	438018	JS	38	MALE	2/3/2019	UNILATERAL [RIGHT]	NR	YES [1000ML/WEEK X 6YEARS]	YES [R.A.]	NO	NEGATIVE	105	180	27
24	719677	DP	49	MALE	1/5/2019	UNILATERAL [RIGHT]	NR	YES [700ML/WEEK X 5YEARS]	NO	NO	POSITIVE	103	200	46
25	718055	SS	69	MALE	29/4/2019	BILATERAL	NR	YES [1500ML/WEEK X 15YEARS]	NO	NO	NEGATIVE	107	115	51
26	291027	SK	32	FEMALE	19/11/2018	BILATERAL	NR	NO	YES [SLE]	NO	POSITIVE	92	230	50
27	708404	LS	40	MALE	7/6/2019	UNILATERAL [LEFT]	NR	YES [1500ML/WEEK X 5YEARS]	NO	NO	POSITIVE	108	163	46
28	693946	PK	68	FEMALE	22/3/2019	UNILATERAL [LEFT]	NR	NO	NO	NO	POSITIVE	92	256	34
29	677765	JS	57	MALE	25/2/2019	UNILATERAL [LEFT]	NR	YES [1500ML/WEEK X 5YEARS]	NO	NO	POSITIVE	97	259	41
30	669600	RS	50	MALE	24/2/2019	UNILATERAL [LEFT]	NR	YES [2500ML/WEEK X 20YEARS]	NO	NO	POSITIVE	108	369	55
31	674218	GSJ	62	MALE	19//2/2019	BILATERAL	NR	YES [1500ML/WEEK X 15YEARS]	YES [BRONCHIAL ASTHMA]	NO	POSITIVE	97	230	45
32	632549	KS	40	MALE	5/12/2018	BILATERAL	NR	YES [1000ML/WEEK X 10YEARS]	NO	NO	POSITIVE	103	92	32
33	772800	PK	45	MALE	22/7/2019	BILATERAL	NR	YES [1000ML/WEEK X 6YEARS]	NO	NO	POSITIVE	92	170	38
34	723082	NS	47	MALE	10/5/2019	BILATERAL	HIV	NO	NO	NO	POSITIVE	98	256	46
35	760128	DR	60	MALE	3/7/2019	BILATERAL	NR	YES [2000ML/WEEK X 10YEARS]	NO	YES	NEGATIVE	92	117	15
36	759977	MK	40	MALE	3/7/2019	BILATERAL	NR	NO	YES [PEMPHIGUS]	NO	POSITIVE	109	230	38
37	385252	BS	70	MALE	3/6/2019	UNILATERAL [RIGHT]	NR	NO	NO	NO	POSITIVE	106	109	45
38	735987	TS	65	MALE	21/6/2019	BILATERAL	NR	NO	YES [BRONCHIAL ASTHMA]	NO	POSITIVE	95	250	45
39	726235	DK	64	MALE	10/5/2019	UNILATERAL [LEFT]	NR	YES [2500ML/WEEK X 10YEARS]	NO	NO	NEGATIVE	109	79	45
40	417021	SB	38	FEMALE	23/1/2020	UNILATERAL [RIGHT]	NR	NO	NO	NO	NEGATIVE	102	249	59
41	688334	K	27	MALE	4/1/2020	BILATERAL	NR	NO	NO	NO	NEGATIVE	93	154	41
42	527829	SK	65	MALE	7/1/2020	UNILATERAL [RIGHT]	NR	NO	YES [BRONCHIAL ASTHMA]	NO	POSITIVE	108	167	44
43	194796	BS	68	MALE	16/3/2020	BILATERAL	NR	YES [1000ML/WEEK X 10YEARS]	YES [BRONCHIAL ASTHMA]	NO	POSITIVE	108	138	33
44	8983388	BY	26	MALE	19/2/2020	BILATERAL	NR	YES [500ML/WEEK X 4YEARS]	YES [BODY BUILDING SUPPLEMENT]	NO	NEGATIVE	97	145	50
45	4487	DS	60	MALE	4/3/2020	UNILATERAL [RIGHT]	NR	YES [1500ML/WEEK X 10YEARS]	NO	NO	POSITIVE	103	160	52
46	779851	AS	51	MALE	2/8/2019	UNILATERAL [LEFT]	NR	YES [500ML/WEEK X 10YEARS]	NO	YES	NEGATIVE	83	200	40
47	912224	GS	44	MALE	6/3/2020	UNILATERAL [RIGHT]	NR	YES [1000ML/WEEK X 10YEARS]	NO	NO	POSITIVE	98	168	22
48	928029	GS	28	MALE	21/5/2020	UNILATERAL [LEFT]	NR	NO	NO	NO	NEGATIVE	92	140	35
49	173444	JS	27	MALE	5/3/2020	BILATERAL	NR	NO	YES [ANKYLOSIS SPONDYLITIS]	NO	NEGATIVE	109	138	37
50	925331	KKJ	56	MALE	6/5/2020	BILATERAL	NR	NO	NO	NO	NEGATIVE	99	59	25
51	546078	KS	37	MALE	10/1/2020	BILATERAL	NR	NO	YES [ANKYLOSIS SPONDYLITIS]	NO	NEGATIVE	98	69	29
52	9669	N	48	FEMALE	25/7/2020	BILATERAL	NR	NO	YES [BRONCHIAL ASTHMA]	NO	POSITIVE	106	214	50
53	7737	JK	36	FEMALE	12/7/2020	UNILATERAL [RIGHT]	NR	NO	NO	NO	NEGATIVE	95	141	45
54	31667	GS	29	MALE	15/2/2020	BILATERAL	NR	YES [1000ML/WEEK X 4YEARS]	YES [BRONCHIAL ASTHMA]	NO	NEGATIVE	109	141	43
55	552703	PC	55	MALE	20/4/2020	BILATERAL	NR	YES [1500ML/WEEK X 10YEARS]	NO	YES	POSITIVE	102	168	38
56	879181	PR	65	MALE	7/2/2020	BILATERAL	NR	YES [2500ML/WEEK X 10YEARS]	NO	NO	NEGATIVE	93	132	37
57	922420	SK	34	MALE	27/4/2020	UNILATERAL [RIGHT]	HBV	NO	NO	NO	POSITIVE	108	179	35
58	12817	SS	30	MALE	17/2/2020	BILATERAL	NR	YES [750ML/WEEK X 3YEARS]	NO	NO	POSITIVE	103	194	51
59	919373	AS	26	MALE	22/6/2020	UNILATERAL [LEFT]	HBV	NO	NO	NO	POSITIVE	96	214	21
60	919043	NM	39	MALE	22/6/2020	UNILATERAL [RIGHT]	NR	NO	NO	NO	POSITIVE	92	299	34

Sr. No	MRD No	Initials	Blood Pressure (SBP) [Normal = less than 130]	Blood Pressure (DBP)[Normal = less than 85]	Fasting Plasma Glucose [Normal = less than 100]	Ficat and arlet classification LEFT SIDE	Ficat and arlet classification RIGHT SIDE	Etiology [Risk Factor For AVN]
1	407605	KS	140	90	90	AVN grade III	AVN grade II	ALCOHOL
2	743993	PS	120	80	95	AVN grade IV	AVN grade IV	STEROID
3	529903	PKS	140	90	95	Normal	AVN grade III	ALCOHOL
4	765325	HD	120	80	98	AVN grade III	AVN grade III	IDIOPATHIC
5	780473	GS	160	90	110	AVN grade III	AVN grade II	ALCOHOL
6	824534	RPS	140	90	95	AVN grade IV	AVN grade II	ALCOHOL
7	829853	SK	120	70	88	AVN grade III	AVN grade II	ALCOHOL, STEROID
8	833190	J	120	70	90	AVN grade IV	AVN grade III	STEROID
9	858575	KD	120	80	84	AVN grade IV	Normal	IDIOPATHIC
10	857249	PS	140	90	110	AVN grade III	AVN grade III	ALCOHOL
11	849692	SK	120	80	120	AVN grade III	Normal	STEROID
12	862534	HK	120	80	79	AVN grade IV	AVN grade II	ALCOHOL, STEROID
13	447492	HK	140	90	90	Normal	AVN grade IV	VIRAL HEPATITIS
14	871040	PD	130	80	98	AVN grade III	AVN grade IV	ALCOHOL
15	867373	RB	150	90	95	AVN grade III	AVN grade II	ALCOHOL,SMOKER
16	598447	LM	140	90	119	AVN grade II	AVN grade IV	ALCOHOL, SMOKER
17	866838	NK	110	70	90	AVN grade III	AVN grade II	STEROID
18	670797	AKG	120	80	90	AVN grade IV	AVN grade IV	ALCOHOL, STEROID
19	803631	KS	120	80	95	AVN grade III	Normal	ALCOHOL
20	594442	SR	120	80	95	Normal	AVN grade IV	IDIOPATHIC
21	678133	GS	120	70	98	AVN grade IV	AVN grade IV	STEROID
22	585467	MK	140	90	90	Normal	AVN grade IV	STEROID
23	438018	JS	130	80	90	Normal	AVN grade IV	ALCOHOL, STEROID
24	719677	DP	150	90	177	Normal	AVN grade IV	ALCOHOL
25	718055	SS	150	90	98	AVN grade III	AVN grade IV	ALCOHOL
26	291027	SK	130	80	90	AVN grade III	AVN grade III	STEROID
27	708404	LS	130	80	95	AVN grade IV	Normal	ALCOHOL
28	693946	PK	140	90	118	AVN grade IV	Normal	IDIOPATHIC
29	677765	JS	130	80	129	AVN grade IV	Normal	ALCOHOL
30	669600	RS	170	90	90	AVN grade IV	Normal	ALCOHOL
31	674218	GSJ	140	90	110	AVN grade II	AVN grade II	ALCOHOL, STEROID
32	632549	KS	150	90	90	AVN grade III	AVN grade II	ALCOHOL
33	772800	PK	120	70	98	AVN grade IV	AVN grade III	ALCOHOL
34	723082	NS	130	80	90	AVN grade IV	AVN grade IV	HIV
35	760128	DR	120	70	90	AVN grade IV	AVN grade IV	ALCOHOL,SMOKER
36	759977	MK	140	80	90	AVN grade III	AVN grade II	STEROID
37	385252	BS	140	90	98	Normal	AVN grade IV	IDIOPATHIC
38	735987	TS	140	90	120	AVN grade II	AVN grade II	STEROID
39	726235	DK	140	80	90	AVN grade IV	Normal	ALCOHOL
40	417021	SB	120	70	90	Normal	AVN grade IV	IDIOPATHIC
41	688334	K	120	70	90	AVN grade III	AVN grade II	IDIOPATHIC
42	527829	SK	135	90	120	Normal	AVN grade IV	STEROID
43	194796	BS	140	90	95	AVN grade IV	AVN grade IV	ALCOHOL, STEROID
44	8983388	BY	120	70	90	AVN grade III	AVN grade II	ALCOHOL, STEROID
45	4487	DS	130	80	98	Normal	AVN grade IV	ALCOHOL
46	779851	AS	140	80	98	AVN grade II	Normal	ALCOHOL, SMOKER
47	912224	GS	135	80	96	Normal	AVN grade III	ALCOHOL
48	928029	GS	120	60	88	AVN grade IV	Normal	IDIOPATHIC
49	173444	JS	110	70	89	AVN grade IV	AVN grade IV	STEROID
50	925331	KKJ	130	85	98	AVN grade IV	AVN grade IV	IDIOPATHIC
51	546078	KS	120	60	89	AVN grade II	AVN grade II	STEROID
52	9669	N	140	90	90	AVN grade IV	AVN grade II	STEROID
53	7737	JK	130	90	97	Normal	AVN grade II	IDIOPATHIC
54	31667	GS	120	70	79	AVN grade III	AVN grade II	ALCOHOL, STEROID
55	552703	PC	140	85	119	AVN grade II	AVN grade III	ALCOHOL, SMOKER
56	879181	PR	150	90	98	AVN grade IV	AVN grade IV	ALCOHOL
57	922420	SK	120	65	94	Normal	AVN grade II	VIRAL HEPATITIS
58	12817	SS	120	65	97	AVN grade III	AVN grade II	ALCOHOL
59	919373	AS	130	85	90	AVN grade IV	Normal	VIRAL HEPATITIS
60	919043	NM	140	90	90	Normal	AVN grade III	IDIOPATHIC

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Date 1.12.19

The Principal,
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Subject: **Approval of Plan of Thesis.**

This is to inform you that the Faculty of Medical Sciences in its meeting held on 29.05.2019 has approved the plan of thesis of **Param Jit Singh**, a student of your college for **MS Orthopaedics** along with the names of Supervisor/Co-Supervisor as under:-

Topic Plan of Thesis

Risk factors of avascular necrosis of femoral head in a tertiary health care

Supervisor
Dr. Harpal Singh Selhi
Prof.,
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Controller of Examinations

Note :

1. *If any discrepancy found regarding topic of thesis or Supervisor/Co-Supervisor, inform undersigned within one month after issue of this letter.*
2. *The student may submit the thesis as per the schedule already conveyed i.e for May/June examination 30th Nov of the preceding the year of examination and for Nov/Dec examinations 31st May of the year of examination.*

RISK FACTORS OF AVASCULAR NECROSIS OF FEMORAL HEAD IN A TERTIARY HEALTH CARE

THESIS PROPOSAL

FOR APPROVAL OF SUBJECT OF THESIS TO BE SUBMITTED

IN PARTIAL FULFILLMENT OF THE REQUIREMENTS

FOR THE DEGREE OF

MASTER OF SURGERY

IN

ORTHOPAEDICS

OF THE

BABA FARID UNIVERSITY OF HEALTH SCIENCES

FARIDKOT

NOVEMBER, 2018 DR. PARAMJIT SINGH

DEPARTMENT OF ORTHOPAEDICS
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ABSTRACT OF PLAN OF THESIS

Title	RISK FACTORS OF AVASCULAR NECROSIS OF FEMORAL HEAD IN A TERTIARY HEALTH CARE
For the degree of	MS ORTHOPAEDICS
Name of the candidate	Dr. Paramjit Singh
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Institution	Dayanand Medical College & Hospital, Ludhiana
University	Baba Farid University of Health Sciences, Faridkot

Introduction: Avascular necrosis of the femoral head is a disabling condition of the hip joint that primarily affects the young individuals. The etiology, natural history, and epidemiology of AVNFH have not been fully elucidated. There are associations of many diseases and drugs with AVNFH. This study is design to look for the risk factors of avascular necrosis of femoral head.

Aims & objectives: to determine risk factors of avascular necrosis of femoral head in a tertiary health care.

Material & Methods: Prospective analysis of pattern of avascular necrosis of femoral head, conducted in patients undergoing treatment at Dayanand Medical College & Hospital. Patient presenting with avascular necrosis of femoral head for period starting from 1st November 2018 to June 2020 will be taken up for study.

Clinical Significance: AVN of femoral head is multifactorial that is associated with genetic predilection and exposure to certain risk factors.These risk factors include chronic corticosteroid administration, chronic alcohol ingestion, smoking, and various chronic diseases .Although the pathophysiologic mechanisms of AVN are inconclusive, growing evidence has supported that several risk factor contribute to the initiation and progression of AVN process. During the past several decades, the general population has experienced remarkable changes in lifestyle as economic development and the ageing process went on. As a consequence, a variety of health problems emerged, such as the increase of the risk factor of Metabolic syndrome and AVN. In the context of AVN of femoral head, studies evaluating the risk factors in these patients as well as delineating correlation are limited. To fill in this knowledge gap, a study of this order is necessary.

Keywords:Avascular necrosis, femoral head, hip joint, risk factor.

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Candidate	Co-supervisor	Co-supervisor	Supervisor	Principal

CERTIFICATE OF FACILITIES AVAILABLE

This is to certify that the facilities for work on the subject of thesis titled **"RISK FACTORS OF AVASCULAR NECROSIS OF FEMORAL HEAD IN A TERTIARY HEALTH CARE"** exist in the Department of Orthopaedics, DMC&H, Ludhiana, and will be provided to the candidate. We will see that the data being included in the thesis are genuine and is collected by the candidate himself under our supervision and guidance.

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Date: 29/12/2018

APPROVAL PROFORMA
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Likely date of appearing in PG examination	JUNE 2021
Date of enrollment	MAY 10, 2018
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1. HOD Pharmacology	1. HOD Physiology
2. HOD Surgery	2. HOD Pathology
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5. Dean Academics	5. HOD Medicine
6. Vice Principal	6. HOD Surgery
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	9. Secretary, IEC
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	12. Principal

Approved: Yes / No

Chairperson
Research Committee

Chairperson
Research Committee

Approved: Yes / ~~No~~

Chairperson
Ethics Committee

Chairperson
Ethics Committee

BABA FARID UNIVERSITY OF HEALTH SCIENCES FARIDKOT

PROFORMA FOR REGISTRATION OF SUBJECT FOR

DISSERTATION

1	NAME OF THE CANDIDATE AND ADDRESS	DR. PARAMJIT SINGH. 4862 A , GURU ARJANDEV NAGAR , PUTLIGARH, AMRITSAR, PUNJAB
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3	COURSE OF STUDY AND SUBJECT	MASTER OF SURGERY, ORTHOPAEDICS
4	DATE OF ADMISSION OF COURSE	10th May, 2018
5	TITLE OF THE TOPIC	RISK FACTORS OF AVASCULAR NECROSIS OF FEMORAL HEAD IN A TERTIARY HEALTH CARE

6. BRIEF RESUME OF INTENDED WORK:

6.1 NEED FOR STUDY

Avascular necrosis of femoral head is a progressive, multifactorial and challenging clinical problem that is on the rise[1,2] mostly affecting the middle aged male population in the most productive age group of 25–50 years. When it occurs in children at the femoral head, it is known as Legg-Calvé-Perthes syndrome. Clinically, AVN is a pathological state with multiple etiologies associated with a reduction in the vascular supply to the subchondral bone of the femoral head. This results in osteocyte death and progressive collapse of the articular surface followed by degenerative arthritis of the hip joint. The severity of this disease resides in the fact that it affects mostly young adults, socially and professionally active and with a great life span, which are initially asymptomatic but will eventually need hip arthroplasty surgery until their 5th decade. In majority of patients, non-traumatic AVN of femoral head is either associated with use of alcohol[3], glucocorticoids presence of hematologic disorders (for example: sickle cell anemia[4], thalassemia, polycythemia, hemophilia, myeloproliferative disorder[5], metabolic disorders (Gaucher disease)[6] as well as conditions such as hypercholesterolemia[7], pregnancy[8], chronic renal failure[9], hyperparathyroidism[10], Cushing's disease[11] etc. In about 30% of patients however, etiology of non-traumatic AVNFH is unclear and hence these are termed Idiopathic.[12] Literature from the western world and Asian countries report chronic alcohol consumption and steroid administration as the most common aetiologies.

Metabolic syndrome is known to be a cluster of interrelated risk factors of metabolic origin such as elevated blood pressures, glucose metabolism

disturbances, dyslipidemia, and obesity.[13] The exact mechanisms of the complex pathways of metabolic syndrome are under investigation. The pathophysiology is very complex and has been only partially elucidated. Most patients are older, obese, sedentary, and have a degree of insulin resistance. Stress can also be a contributing factor. The most important risk factors are diet (particularly sugar-sweetened beverage consumption), genetics, aging, sedentary behavior or low physical activity, disrupted chronobiology/sleep, mood disorders/psychotropic medication use, and excessive alcohol use.

Definitions of metabolic syndrome :-

IDF (International Diabetes Federation)

According to the new definition, for a person to be defined as having the Metabolic syndrome, they must have central obesity (defined as waist circumference :-Male ≥ 90 cm & Female ≥ 80 cm) plus any two of four additional factors. These four factors are:

1. Raised triglycerides: > 150 mg/dL (1.7 mmol/L), or specific treatment for this lipid abnormality
2. Reduced HDL cholesterol: < 40 mg/dL (1.03 mmol/L) in males, < 50 mg/dL (1.29 mmol/L) in females, or specific treatment for this lipid abnormality
3. Raised blood pressure (BP): systolic BP > 130 or diastolic BP >85 mm Hg, or treatment of previously diagnosed hypertension
4. Raised fasting plasma glucose (FPG): >100 mg/dL (5.6 mmol/L), or previously diagnosed type 2 diabetes

WHO

The World Health Organization 1999 criteria require the presence of any one of diabetes mellitus, impaired glucose tolerance, impaired fasting glucose or insulin resistance, AND two of the following:

1. Blood pressure: ≥ 140/90 mmHg
2. Dyslipidemia: triglycerides (TG): ≥ 1.695 mmol/L and high-density lipoprotein cholesterol (HDL-C) ≤ 0.9 mmol/L (male), ≤ 1.0 mmol/L (female)
3. Central obesity: waist:hip ratio > 0.90 (male); > 0.85 (female), or body mass index > 30 kg/m2
4. Microalbuminuria: urinary albumin excretion ratio ≥ 20 μg/min or albumin:creatinine ratio ≥ 30 mg/g

The global burden of Metabolic Syndrome is 20-25% [14] and in India the prevalence is 19%. The metabolic syndrome is associated with a 2-fold increase in cardiovascular outcomes and a 1.5-fold increase in all-cause mortality.[15]

Intriguingly enough, in the context of AVN, studies looking at risk factor associated with AVN of femoral head in these patients as well as delineating correlation are limited. To fill in this knowledge gap, a study of this order is necessary. Thus a study design to study the possible risk factor of avascular necrosis of the femoral head is necessary because very few such studies has been done in India especially. Being the tertiary care hospital and as a referral hospital for several district hospital, it represents the pattern of AVN of femoral head in indian population.

6.2 REVIEW OF LITERATURE

In a study Byzhao et al analysis showed that high blood levels of triglycerides, total cholesterol, LDL-cholesterol, and non-HDL-cholesterol, male, urban residence, family history of osteonecrosis of the femoral head, heavy smoking, alcohol abuse and glucocorticoid intake, overweight, and obesity were all significantly associated with an increased risk of AVN of femoral head.[16]

Puhl et al studied 100 cases and found disturbance of lipid metabolism, found in 41% of the patients, deviation of the liver function data, and, finally, abuse of alcohol as discovered on the basis of the case history. The statistically significant correlation of these factors makes it probable that there is actually a pathogenetic chain abuse of alcohol--hyperlipoproteinemia--arteriosclerosis--osteonecrosis.[17]

De Bastiani et al found the statistical data that were analysed confirmed the role of some of the etiological factors concerned. A long-term study was also undertaken, with a preliminary follow-up at 22 months, on the progress of the patients with monolateral idiopathic osteonecrosis of the femoral head who were subjected to a therapeutic programme of dietary correction and the administration of medicaments.[18]

Koch et al studied about 70 patients with necrosis of femoral head. In 28 patients found anamnestic hints to large-dose steroid therapy, chronic alcoholism or radiation. As a result of the biochemical blood examination in 29 patients hyperlipoproteinemia and in 25 patients dyslipidemia were determined, accompanied by a carbohydrate metabolic disturbance (15 cases) and a purine metabolic disturbance (13 cases). The statistically

significant correlation of these factors makes it probable that there is actually a pathogenetic chain abuse of alcohol--hyperlipoproteinemia--arteriosclerosis--osteonecrosis. No specific importance of the uric acid and glucose metabolism could be established, since the metabolic disturbances associated with these processes are mostly linked with the observed hyperlipoproteinemia [19]

Zsernaviczky J et al studied the relation between aseptic necrosis of the femoral head and the primary disturbance of fat metabolism type II hypercholesterinemia. Type II hypercholesterinemia is of particular importance since it produces early atheriosclerosis which demands early diagnosis, since this condition associated with aseptic necrosis of the femoral head.[20]

Gold EW and Cangemi PJ in 1979 presented a report on incidence and pathogenesis of alcohol-included osteonecrosis of the femoral head.[21] In this study 790 patients admitted for treatment of alcoholism were examined for evidence of osteonecrosis of the femoral head. Lab data of these patient shows average serum cholesterol levels were within normal limits and average serum triglyceride levels were moderately elevated only in those individuals classified as having a severe addition to alcohol. Two patients was found to have advanced idiopathic bilateral osteonecrosis of the femoral head. One of these patients had undergone one total hip replacement prior to his current admission. This study indicates that there is a very low incidence of osteonecrosis among alcoholics (less than 0.3%), Alcoholism lead to lipid dysfunction that causes osteonecrosis in certain predisposed individuals. A combination of several factors such as systemic fat embolism, elevated circulating levels of inflammatory fatty acids or prostaglandins and

osteoporosis and charcot-like effects, which are also associated with corticosteroid-included osteonecrosis, seem to be involved and may contribute, as well, to other instances of femoral head osteonecrosis.

Jacobs B, took 164 patients with alcoholism-induced osteonecrosis in his study over a 22-year period, from 1962 to 1984. In this study The presence of femoral head necrosis was diagnosed in patients aged 21-67 years; 28% of patients were under 40 years of age and 76% were under 50 years . Bilateral hip necrosis was present in 44.5% of patients and, within three years of the diagnosis with necrosis of femoral head, the presence of multifocal necrosis became evident in 23 cases at sites away from the hip (shoulders and knees). Hyperlipidemia was found in 38.4% of cases, involving both cholesterol and triglycerides. This paper supports the hypothesis that co-existent hyperlipidemia is linked to alcoholism induced bone necrosis.[22]

Kuga Y. in 2000 published his study on the factors associated with osteonecrosis in the femoral head in chronic alcoholism.[23] These results suggested that osteonecrosis occurred in the late stages of liver disease when serum enzyme concentrations had returned to normal or were only mildly elevated.

You-chen chao at al[3] in 2003 reported presence of alcohol metabolizing enzyme genes in chinese alcoholics with avascular necrosis of the hip joint , pancreatitis and cirrhosis of the liver . it was concluded that there are multiple theories about the pathogenesis. Two of them are commonly mentioned 1) thromboemboli in the blood supply to bone resulting from circulating fat and 2) vessel occluded by excessive packing of the adjacent marrow spaces with extravasated blood or fat. This paper supports the hypothesis that the

presence of dysfunction of carbohydrate and lipid metabolism was more prevelant in patient with osteonecrosis of bone and alcohol induced liver disease.

6.3 AIMS AND OBJECTIVES OF THE STUDY

- To determine the risk factors associated with the development of avascular necrosis of the femoral head.

syndrome will be done according to IDF and WHO classification of metabolic syndrome All the data will be filled up in a proforma.

Nowadays, there are more than 16 different classification systems used to classify and describe aseptic necrosis of the femoral head, from which the classification system introduced by Ficat is the most commonly used.

Ficat and arlet classification of avascular necrosis of femoral head.

0	Inconspicious/normal findings
I	Inconspicious findings or minor changes (slight patchy osteoporosis, blurring of trabecular pattern, subtle loss of clarity)
II A	Diffuse/ focal radiological changes (osteoporosis, sclerosis, cysts)
II B	Subchondral fracture ("crescent sign") segmental flattening of femoral head ("out-of-round appearance")
III	Broken contour of femoral head, bone sequestrum, joint space normal
IV	Flattened contour of femoral head, decreased joint space collapse of femoral head, acetabularosteoarthrotic changes

Waist circumference measurement:

The waist circumference should be measured at the midpoint between the lower margin of the last palpable ribs and top of the iliac crest ,using a stretch resistant tape that provides as constant 100g tension.Hip circumference should be measured around the widest portion of the buttocks, with the tape parallel to the floor.

Inclusion Criteria:

Men or women > 18 yrs and above age with features of AVN of femoral head

Exclusion Criteria:

- Fractures of the acetabulum, femoral head and neck of femur.

- Dislocation of hip joint.
- Diagnosed neoplastic condition.
- Immune compromised conditions.
- Septic arthritis of hip joint
- Osteomyelitis of proximal femur
- Osteomyelitis of pelvis.

OUTCOME

This study will analysis the risk factors associated with the development of avascular necrosis of the femoral head

STATISTICAL ANALYSIS

Data will be described in terms of range; mean ±standard deviation (± SD), median, frequencies (number of cases) and relative frequencies (percentages) as appropriate. All statistical calculations will be done using SPSS (Statistical Package for the Social Science) SPSS 21 version statistical program for Microsoft Windows.

7.3 DOES THE STUDY REQUIRE ANY INVESTIGATIONS OR INTERVENTIONS TO BE CONDUCTED ON PATIENTS OR OTHER HUMANS OR ANIMALS? IF SO, PLEASE DESCRIBE BRIEFLY.

No special investigation.

7.4 Has the ethical clearance been obtained from ethical committee of your Institution in case of 7.3?

Yes, attached herewith.

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PROFORMA

S.NO

NAME AGE/ SEX

MRD NO ADMISSION NO

DATE OF ADMISSION DATE OF DISCHARGE

RELIGION

JOINT (LEFT/ RIGHT)

UNILATERAL/ BILATERAL

HISTORY OF TRAUMA YES/ NO

INVESTIGATION:

HB

TLC

PLT

UREA

CREATININE

PT/ INR

VIRAL MARKER

X RAY (PBH)

MRI REPORT OF HIP JOINT

ALCOHOL CONSUMPTION

PROTEIN OR DIETARY SUPPLEMENTS

STEROID USE/ABUSE (INDICATION ,REGIME AND DOSAGE)

INVESTIGATION FOR SPECIFIC DISEASE

Signature of Candidate **Signature of Supervisor**

Metabolic profile

IDF Classification:-

Central obesity : Waist circumference

	< 90 cm	>90 cm
Males		

	< 80 cm	> 80 cm
Females		

And any two of the following :-

		Remarks
Triglycerides:	<150 >150	
HDL Cholesterol	>40 <40	
Blood Pressure (BP)	<130/85 >130/85	
Fasting Plasma Glucose:	<100 >100	

Signature of Candidate **Signature of Supervisor**

WHO Classification

Impaired glucose tolerance/DM Present Absent

And any two of the following:

		Remarks
1. **Blood Pressure (BP)**	<140/90	
	> 140/90	
2. **Dyslipidaemia:**		
TG	<1.695	
	>1.695	
HDL-C	>0.9	
	<0.9	
3. **Central Obesity**		
Waist Hip Ratio	<0.90 (M) >0.85 (F)	
	<0.90 (M) >0.85 (F)	
4. **Microalbuminuria**		
Urinary albumin creatinine ratio	<20 >20	

MRI Classification (Ficat and arlet classification):

Signature of Candidate **Signature of Supervisor**

INFORMED PATIENT CONSENT

Date: _____

I.....D/o, W/o, S/o.....

am willing to participate in the study **'RISK FACTORS OF AVASCULAR NECROSIS OF FEMORAL HEAD IN A TERTIARY HEALTH CARE'** The procedure with its complications has been explained to me in local vernacular language. I have fully understood that no special tests and extra expenditure in any form, merely for the purpose of thesis is being carried out. I am free to opt out the study any time without assigning any reason.

.....
Signature of the Witness

Name:

.....
Signature of the patient

Signature of Candidate

Signature of Supervisor

मरीज अनुमति फार्म

तिथि _____

मैं _____ पत्नी/पुत्र/पुत्री _____ निवासी _____ इस शोधकार्य **'RISK FACTORS OF AVASCULAR NECROSIS OF FEMORAL HEAD IN A TERTIARY HEALTH CARE'** में भाग लेने के लिए सहमत हूँ। मैं इस शोधकार्य में भाग लेने के लिए अपनी स्वेच्छा से तैयार हूँ। मैं पुष्टि करता/करती हूँ की यह स्वीकृति देने के लिए मुझे कोई आर्थिक प्रलोभन नहीं दिया गया और न ही दबाव डाला गया है। मुझे इस शोधकार्य का उद्देश्य स्पष्ट कर दिया गया है और मुझे यह विश्वास है की यह विज्ञान और मानवता के लाभ के लिए है। मुझे इस शोधकार्य में होने वाले जोखिम के बारे में समझा दिया गया है और मेरी समझ में यह जोखिम बहुत मामुली है।

मैं इस शोधकार्य में भाग लेने के सम्बन्ध में किसी भी समय अपनी अस्वीकृति व्यक्त कर सकता/सकती हूँ और मेरे अस्वीकृति व्यक्त करने का मेरे इलाज पर कोई प्रभाव नहीं पड़ेगा।

_____
गवाह के हस्ताक्षर
नाम:

_____
रोगी के हस्ताक्षर/अंगूठे का निशान
नाम:

_____
अन्वेषक के हस्ताक्षर

_____
विद्यार्थी के हस्ताक्षर

ਮਰੀਜ਼ ਰਜ਼ਾਮੰਦੀ ਫ਼ਾਰਮ

ਮਿਤੀ_____

ਮੈ_____ਪਤਨੀ/ਪੁੱਤਰ/ਪੁੱਤਰੀ_____

ਵਾਸੀ _____

'RISK FACTORS OF AVASCULAR NECROSIS OF FEMORAL HEAD IN A TERTIARY HEALTH CARE' ਤੇ ਚਲ ਰਹੀ ਖੋਜ ਵਿਚ ਹਿੱਸਾ ਲੈਣ ਲਈ ਰਜ਼ਾਮੰਦ ਹਾਂ। ਇਸ ਖੋਜ ਕੰਮ ਵਿਚ ਹਿੱਸਾ ਲੈਣ ਲਈ ਮੈ ਆਪਣੀ ਮਰਜ਼ੀ ਨਾਲ ਤਿਆਰ ਹਾਂ। ਮੈ ਇਹ ਦਸਣਾ ਚਾਹੁੰਦਾ ਹਾਂ/ ਚਾਹੁੰਦੀ ਹਾਂ ਕੇ ਇਹ ਰਜ਼ਾਮੰਦੀ ਦੇਣ ਵਾਸਤੇ ਮੈਨੂ ਕਿਸੇ ਵੀ ਤਰਾਂ ਦਾ ਲੋਭ-ਲਾਲਚ ਨਹੀ ਦਿੱਤਾ ਗਿਆ ਅਤੇ ਨਾ ਹੀ ਕੋਈ ਦਬਾ ਪਾਇਆ ਗਿਆ ਹੈ। ਮੈਨੂ ਇਸ ਖੋਜ ਦਾ ਮਨੋਰਥ ਸਮਝਾ ਦਿੱਤਾ ਗਿਆ ਹੈ ਅਤੇ ਮੈਨੂ ਇਹ ਭਰੋਸਾ ਦਵਾਇਆ ਗਿਆ ਹੈ ਕੇ ਇਹ ਖੋਜ ਵਿਗਿਆਨ ਅਤੇ ਮਾਨਵਤਾ ਦੀ ਭਲਾਈ ਲਈ ਹੈ। ਮੈਨੂ ਇਸ ਖੋਜ ਵਿਚ ਹੋਣ ਵਾਲੇ ਖਤਰੇ ਬਾਰੇ ਸਮਝਾ ਦਿੱਤਾ ਗਿਆ ਹੈ ਅਤੇ ਮੈਨੂ ਇਹ ਯਕੀਨ ਹੈ ਕੇ ਇਹ ਖਤਰਾ ਬਹੁਤ ਮਾਮੂਲੀ ਹੈ। ਮੈਨੂ ਇਸ ਖੋਜ ਕੰਮ ਵਿਚ ਹਿੱਸਾ ਲੈਣ ਦਾ ਢੰਗ – ਤਰੀਕਾ ਸਮਝਾ ਦਿੱਤਾ ਗਿਆ ਹੈ।

ਮੈ ਇਸ ਖੋਜ ਕੰਮ ਵਿਚ ਹਿੱਸਾ ਲੈਣ ਬਾਰੇ ਆਪਣੀ ਰਜ਼ਾਮੰਦੀ ਕਿਸੇ ਵੀ ਸਮੇ ਵਾਪਸ ਲੈ ਸਕਦਾ ਹਾਂ/ ਸਕਦੀ ਹਾਂ ਅਤੇ ਮੇਰੀ ਰਜ਼ਾਮੰਦੀ ਵਾਪਸ ਲੈਣ ਦਾ ਮੇਰੇ ਇਲਾਜ ਤੇ ਕੋਈ ਅਸਰ ਨਹੀ ਹੋਵੇਗਾ।

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ਗਵਾਹ ਦੇ ਹਸਤਾਖਰ ਮਰੀਜ਼ ਦੇ ਹਸਤਾਖਰ

ਮਿਤੀ_____ ਮਿਤੀ_____

ਪਤਾ _____ ਪਤਾ _____

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ਨਿਰੀਖਕ ਦੇ ਹਸਤਾਖਰ

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ਸਿਖਿਆਰਥੀ ਦੇ ਹਸਤਾਖਰ